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THE BLOOD SUPPLY OF THE THYROID GLAND
II. THE NODULAR GLAND

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THE thyroid gland, its physiology and its pathology have formed the basis of several careful experimental studies over many years. It is now well recognized that the activity and morphology of the thyroid epithelium can be influenced by a wide variety of changes in the environment of the experimental animal. Thus hyperplastic changes can be induced in the thyroid cells by feeding the animal on an iodine deficient diet, by giving the animal drugs of the thiourea group, or by the administration of thyroid-stimulating hormone.

On surveying these stimuli it is seen that they must produce their action on the gland by way of the blood stream and one might reasonably expect that they would produce a uniform effect. Now in practice it is known that uniform changes do occur in the thyroid gland on many occasions. It is, however, more common for the effect produced to be patchy in distribution — the result being a nodular goitre.

It will be realized that the problems posed by the aetiology of nodules in the thyroid are merely specific examples of a general problem in pathology. In the breast and in the uterus one sees similar examples: in these sites local nodules of hyperplastic tissue develop under the influence of changes in the blood hormonal level—a local manifestation of what is presumably a general stimulus.

In parathyroid hyperplasia, a disease in which changes in hormone and electrolyte levels can be detected (all in the blood stream), one often observes that the changes in bone are localized to an unexpected degree. When the pathological changes of necrosis in liver and kidney and the subsequent cirrhosis or chronic nephritis are examined it is seen that, here again, are examples of a blood-borne stimulus giving patchy changes—in these cases those of tissue damage. That the initial change was, in fact, irregular in distribution is evident on examination of the nodules of regenerating liver tissue or of hyperplastic renal tubules.

There are at least two possible explanations of this phenomenon whereby a blood-borne stimulus may produce an irregular response. They are:—

(1) that the cells on which the stimulus acts may not be equally influenced by that stimulus and, therefore, some groups of cells alter to a greater degree than do their neighbours;

(2) that, although the stimulating agent is of uniform concentration in the blood stream, because of variations in blood flow to various areas in the tissue, it reaches different groups of cells in different concentrations.

The second possibility clearly raises the question of blood supply to the normal tissue and its variations under pathological conditions. With these ideas in mind the blood supply of the thyroid has been investigated: the blood supply to the normal gland formed the initial part of this study (Johnson, 1953). In this paper, some of the variations from normal seen in the nodular gland are discussed.

HISTORICAL SURVEY

Although much work has been carried out on the thyroid gland the question of its blood supply has received but scant attention: particularly does this apply to the vessels of the pathological gland. It is of interest to note that Anna Bégoune (1884), one of the earliest investigators to attack the problem of thyroid vasculature, noted that the blood supply to thyroid nodules was relatively less than that to the gland in general. She also observed that the pattern of the blood vessels in the uniformly hyperplastic gland and in the colloid goitre showed no great variation from that which she regarded as normal.

Horne (1892) in studying histological sections of nodular goitres described small intimal pads projecting into the lumen of the intra-glandular arteries in nodular goitre. These, he claimed, were not present in the vessels of the normal gland, nor were they present in other types of pathological thyroid. His claims have not found general acceptance.

Terry, in 1922, described experiments in which he injected various substances into the vessels of the nodular thyroid. After injection and fixation he studied the blood supply of the thyroid nodule and concluded that the nodule received numerous branches from the many vessels which are to be observed in its capsule. As will be seen later the present experiments do not support this notion. Terry also described the histology of the intra-nodular vessels and claimed that they showed considerable variation from normal, particularly in the thickness and composition of the medial coat of the arteries.

Wangensteen (1929), whilst working in De Quervain's clinic in Berne, investigated the thyroid vessels in cretins. In a most interesting paper he describes cases of long-standing goitre in which at operation the inferior thyroid artery was found to be equal in diameter to the common carotid artery. Within the nodules of these highly vascular goitres he describes giant sinudoidal vessels similar to those found in the present series of experiments. Boyd (1947) also makes mention of these large dilated vessels which he states occur frequently in nodular goitres.

The vessels of the hyperplastic gland are more difficult to study effectively since suitable material is less readily available. Operative material is unsatisfactory for this purpose because it cannot be injected adequately and it is rare to see a case of thyrotoxicosis at post-mortem. Lewis-Thomas (1945) and Williams (1937) have, to some extent, overcome these difficulties by the use of the experimental animal. Using rats and rabbits they were able to induce hyperplasia by the use of anti-thyroid drugs and to observe the changes in the capillary bed.

MATERIAL

The material used in these experiments consisted of 28 nodular glands obtained at post-mortem and at operation. For the reasons described previously (Johnson, 1953) operative specimens were found to be unsuitable for investigation by injection methods but were used for macroscopic and microscopic dissection. In the series all stages of nodule formation were observed, ranging from small, single nodules in otherwise normal glands to multiple, large nodules involving almost all of the glandular tissue.

The methods of investigation used included routine histological examination and injection with carmine-gelatine and barium-gelatine, the injected glands being then examined by the thick frozen-section technique. The details of these methods have been fully dealt with in a previous publication (Johnson, 1953). It is important to realize, that, unless otherwise stated, all the illustrations are of sections 150 μ in thickness.

RESULTS

The normal gland

As has already been pointed out, the thyroid gland is essentially lobular. The blood supply to the normal organ is therefore of lobular distribution; and progressive branching of vessels may be observed until a small artery ultimately enters the thyroid lobule. In the course of this branching we may recognize branches of the following order:—

(i) main arteries — running on the surface gland;

(ii) interlobar arteries—running between structural lobes; giving branches to lobes and then dividing into

(iii) interlobular arteries — running into lobes and between lobules; and giving off

(i) lobular arteries, which supply the thyroid lobule.

Anastomoses between the arteries occur both on the surface and in the depths of the gland, and there is some evidence for the occurrence of arterio-venous shunts within the substance of the thyroid. Further details of this supply have been given previously (Johnson, 1953).

The developing nodule

In attempting to follow the evolution of the thyroid nodule, comparatively little is gained by examination of the late examples of the condition. By the time that multiple large nodules have appeared, various degenerative changes have occurred within the nodules and have masked both the traces of their own development and that of their blood supply. If, however, one examines a series of nodular thyroids, starting from those which show the most minimal change and progressing to those which show maximum change, certain features become clear. (In point of fact it was easier in practice to work backwards in this series, because in so doing one begins with a well-recognized entity.)

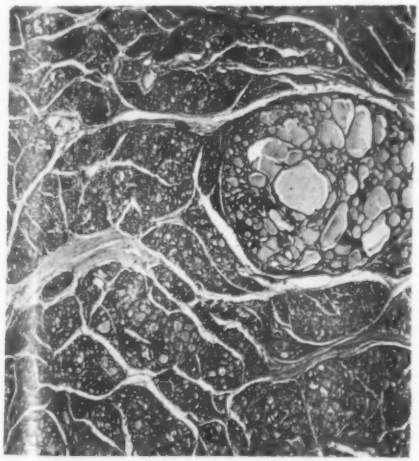

FIG. I. Photomicrograph of a section of thyroid gland; the lobules are separated from each other by a small amount of connective tissue. One lobule is larger than its companions and is, in fact, a small nodule. (x 25) (7μ)

Considering a single nodule, in the most advanced cases its morphology is that of a large group of vesicles aggregated into a mass of tissue and surrounded by a thick fibrous capsule. Now on examining smaller and smaller nodules (and therefore presumably nodules at an earlier stage of their evolution) one observes two general trends of change:—

(a) the number of vesicles making up the nodule become progressively less and less until it approaches the number found in a normal thyroid lobule;

(b) the amount of connective tissue in the capsule decreases progressively until ultimately it is no more obvious than that which surrounds the normal lobule of the thyroid gland.

FIG. 11. Photograph of the cut surface of an "oedematous" thyroid gland in which there are many small nodules. Close inspection will show that the smallest nodules distend structural lobes. (x ½)

On examining sections of very small nodules (Fig. I) it becomes apparent that they are, in fact, merely large lobules.

These small nodules can be observed macroscopically. By perfusion of the thyroid with normal saline for a period of thirty minutes it is possible, by rendering the tissue grossly oedematous, to separate the structural

lobes from each other. If this is done in a nodular gland, close inspection of its cut surface will show the enlarged lobules distending the structural lobes (Fig. II). The conclusion is thus reached that a nodular goitre arises by the progressive increase in size of many of its component lobules.

and should many lobules progressively enlarge, the result is the fully developed nodular goitre. These facts are shown diagrammatically in Fig. III.

It has already been shown that the lobule receives its own small artery and vein. Section of an injected gland containing small

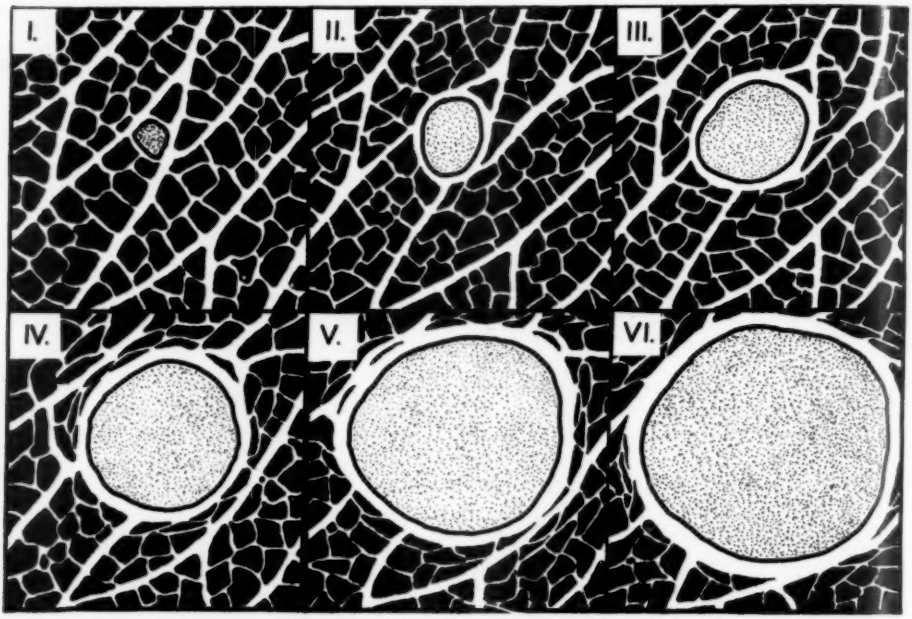

FIG. III. Diagram of a series of sections of thyroid tissue. In (I) each individual solid black area represents a thyroid lobule. These are grouped together to form structural lobes. There is only a small quantity of fibrous tissue (white in the diagram) between the lobules and slightly more fibrous tissue between the lobes. One lobule, as is shown, enlarges progressively to form the thyroid nodule.

In (II), (III) and (IV) as a nodule enlarges there is distortion and compression of the surrounding thyroid lobules and, associated with this, there is an increase in the amount of fibrous tissue around the nodule.

In (V) and (VI) some of the lobules have disappeared completely and, as is to be expected, there is a still further increase in peri-nodular fibrous tissue.

Changes in the size of the lobules in the thyroid gland may occur under a variety of stimuli. This change in size may be associated with hyperplasia or with involution in the vesicles which make up the lobules. From the present point of view, the change in size is the important factor.

Now if this lobular change affects the gland diffusely, a diffuse hyperplastic goitre or a colloid goitre is the result; but should the change in size affect one lobule more than its neighbours, then a small nodule develops

nodules will show that they possess their own separate vascular bed (Fig. IV). Moreover, if one is fortunate enough to cut the section in the plane of the lobular vessel, the small artery to the nodule may be observed.

When the nodule becomes somewhat larger, it is found that it can be shelled out of the gland, providing that the correct plane between nodule and surrounding tissue is entered. On attempting this, one may observe a vessel crossing the plane and entering the nodule — this vessel is the lobular or, low,

rather the "nodular" artery. Growth of the nodule may distort the normal anatomy somewhat and may separate artery and vein to some extent.

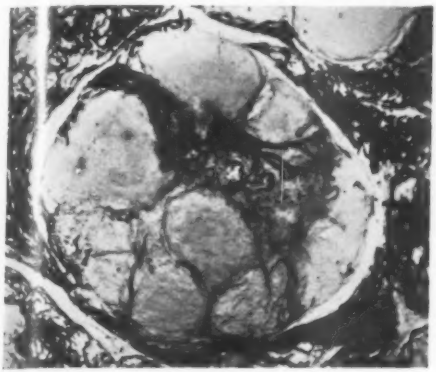

FIG. IV. Photomicrograph of a section of an injected thyroid gland. A small nodule, the vascular bed of which is separate from that of the neighbouring lobules, may be observed. (x 50)

In this series of experiments many nodules have been shelled out of their surrounding capsule. It has been found easier to do this with fresh than with fixed specimens. The nodules shell out readily when they are small and are attached merely by a fine band of connective tissue containing their artery and vein; but, as they become larger, and particularly if they show degenerative changes and associated inflammation in the wall, they become adherent to their capsules.

Vascular pattern in nodule

Clearly as a nodule enlarges, new vessels must develop to supply the increase in amount of parenchymatous tissue.

Let us pause to consider the morphology displayed by the nodule as it increases in size. The increase in bulk of tissue is due to the formation of many new vesicles and, as these vesicles develop, they form a pattern within the nodule. Individual vesicles or groups of vesicles may show the characters of either hyperplasia or of involution, but, for the moment, this may be ignored since the point in question is the overall architecture of the nodule.

FIG. V. Photomicrograph of a section of injected thyroid gland. A sector of a thyroid nodule is seen in the lower right hand quadrant of the photograph; there is a space between this nodule and its capsule and, crossing that space, the artery of supply to the nodule can be seen. (x 100)

When examined either macroscopically or microscopically, no evidence of the development of new lobules within the nodule can be found. This is a matter of simple observation which can be made by examining any series of nodular goitres. The injected nodule correspondingly shows a more simple vascular bed than that seen in the adult gland (Figs. VI, VII, VIII). Arteries radiate out from its hilum and run between groups of vesicles. Branches are given off to these vesicles in an irregular fashion and no lobular pattern can be seen in the vascular bed of the nodule. Sometimes however, crude attempts at lobular pattern may be observed but these are not distinct enough to form definite lobules.

The capillary bed within the nodule, like that within the gland, varies in its pattern with the cellular activity in the vesicle. In general, the capillaries can be observed to form a plexus surrounding the individual vesicles. The labile nature of the capillary bed in thyroid tissue has been well demonstrated by Williams (1944). He studied thyroid vesicles in a transparent chamber in the rabbit's ear and noted great variation in the capillary bed with changes in cellular activity.

Occasionally groups of nodules within a common capsule may be seen in the thyroid gland. In such circumstances each nodule

represents an enlarged lobule and the external capsule surrounding them is the fibrous septa around the structural lobes. In these cases a group of lobules has enlarged in the structural lobe and gives rise to the picture of nodules within a capsule.

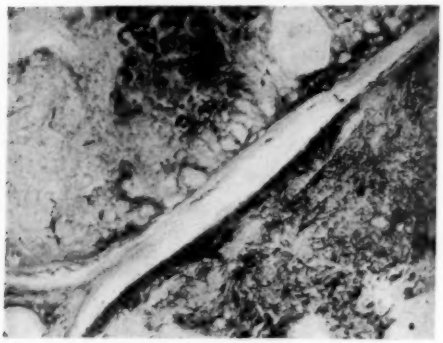

FIG VI. Photomicrograph of a section of injected nodular goitre. Segments of two large nodules are shown. In the lower right hand nodule the vascular bed is filled but the lack of lobular pattern may be clearly seen. In the upper left hand nodule there is a collection of giant vessels and it can be seen that they are the only part of the bed filled with the injection medium. Compare Fig. VIII. (x 12)

It may be stated then, that the developing nodule fails to reproduce the complex architecture of the adult gland and that there is an associated failure to develop the complex vascular pattern.

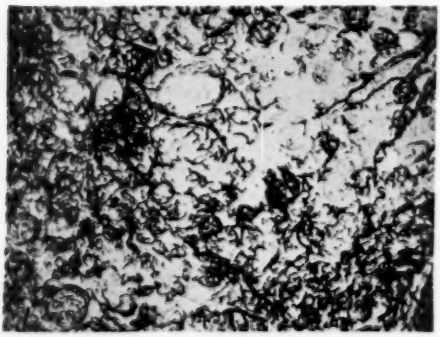

FIG. VII. Photomicrograph of the same section of the injected gland shown in Fig. VI. Here, under higher power, the vascular bed of the nodule may be more closely observed and the lack of lobular pattern seen. Compare Fig. VIII. (x 25)

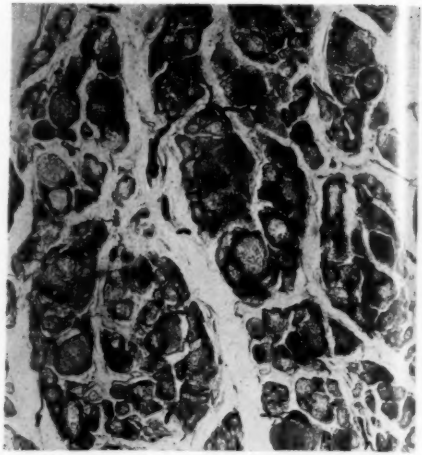

FIG. VIII. Photomicrograph of a section of injected normal thyroid gland. The lobular pattern is quite clear. This photograph is shown for comparison with Figs. VI and VII. (x 12)

The changes in the vascular bed of tissues surrounding the nodule

If one observes the thyroid tissue surrounding a developing nodule it is found that the vesicles progressively diminish in size and finally disappear. Not only do vesicles disappear but also lobules and sometimes structural lobes follow suit. There develops *pari passu* with this change, an increase in the amount of connective tissue around the nodule, and in some long-standing nodules there may ultimately develop a thick layer of peri-nodular fibrous tissue.

On dissecting a nodule out of its bed one is impressed by the presence of numerous large vessels in this surrounding connective tissue. They can be seen by the naked eye and in the uninjected specimen. However, by studying the injected nodular gland the significance of these large vesels becomes apparent. As might be expected, associated with the disappearance of the vesicles, one finds that the capillary bed disappears (Fig. IX). However, the major vessels such as the interlobular and interlobar arteries disappear at a slower rate than do the capillaries and they persist in the tissue surrounding the nodule (Fig. X).

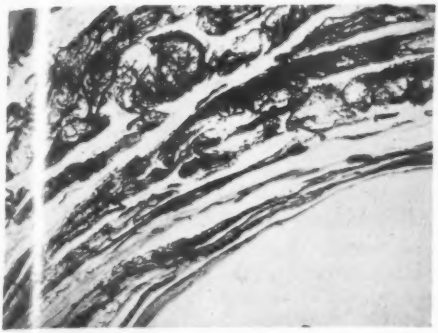

FIG. IX. Photomicrograph of a section of injected thyroid gland. The vascular bed in the tissues surrounding a nodule (which has fallen out of the section) is seen. The progressive disappearance of the capillary bed as one passes in toward the nodule is well shown. (x 25)

If the section happens to cut the tissue surrounding a large nodule in a tangential fashion one may observe the pattern of blood vessels in this area in more detail. When this is done (Fig. X) it is seen that the vascular bed which intervenes between the arteries and veins has changed its pattern completely and now consists of a simple capillary plexus without any suggestion of lobular or vesicular arrangement.

FIG. X. Photomicrograph of a section of injected nodular goitre. The capsule of a nodule has been cut tangentially. Note the simple pattern of the vascular bed in the capsule (that is, the lack of lobular pattern). (x 50)

Thus the significance of the larger vessels referred to above becomes apparent. They are merely the interlobular and lobular arteries and veins which persist when the capillary bed becomes simplified and thereby become relatively more obvious.

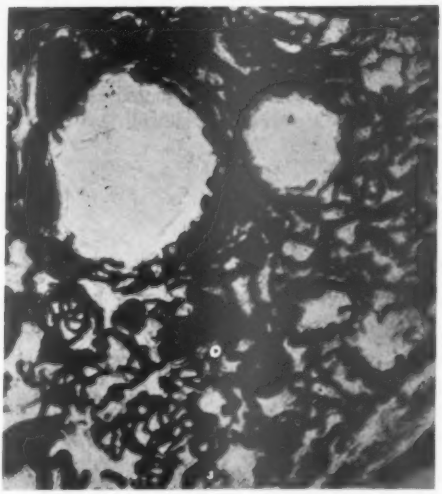

FIG. XI. Photomicrograph of a section of injected nodular goitre showing a group of dilated tortuous vessels. (x 50)

Now, if the nodule should become necrotic, as is often the case in old standing nodular goitres, the pattern of the surrounding vessels is seen to change. Usually such nodules are surrounded by a dense layer of fibrous tissue and it is found the nodule can no longer be shelled out of the surrounding gland. In cases such as this, numerous small vessels may be seen passing across the fibrous tissue layer and into the nodule. These presumably represent newly-formed vessels which developed as the nodule became necrotic and which grew from the surrounding gland into the nodule. The point to realize is that the simple lobular nature of the blood supply to the nodule may be lost when such changes as cyst formation, haemorrhage and necrosis occur in that nodule, being obscured by inevitable complexities of structure associated with tissue (and vascular) changes of degenerative and proliferative (reactionary) kind.

Changes in the intra-nodular vessels

In this series of experiments two types of changes have been observed in the intra-nodular vessels. They are:—

(i) Modification of the pattern in hyperplastic areas

As is well known, small areas of hyperplasia may often be observed within a thyroid nodule, and associated with the increase in number and activity of the thyroid cells there is an increase in the size and number of blood vessels in the area. The extent of this vascularity cannot be appreciated by examining routine histological material.

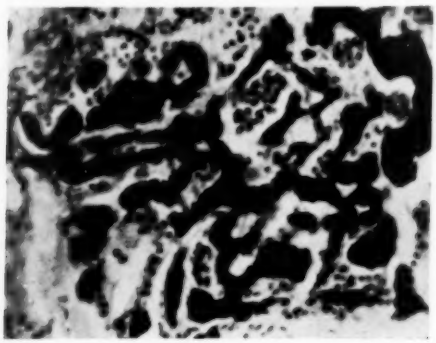

FIG. XII. Photomicrograph of a section of injected nodular goitre. This section is prepared in the routine fashion after injection. Whilst the cytological detail is poor, the general association of dilated capillary sinusoids to the column of cells may be made out. This section was taken from the same area as is seen in Fig. XI. (x 200) (7μ)

The vesicular pattern is often lost and it may be seen that there develops a tortuous mass of blood vessels in the hyperplastic area (Fig. XI). In an attempt to show the relation of these tortuous vessels to the thyroid cells some routine histological sections were prepared of these hyperplastic areas. Unfortunately, having subjected tissues to the insults of perfusion, they are no longer capable of giving high class cytological detail. However, as can be seen (Fig. XII), the general pattern can still be determined. In injected material the vessels are much more obvious and many dilated sinusoidal capillaries are observed running between the groups of thyroid cells.

(ii) Development of giant vessels

Occasionally in injected nodules giant sinusoidal vessels may be observed (Fig. XIII). These occur in groups throughout the nodule and are found to consist of many wide, thin-walled, tortuous vessels. Vessels of arterial and capillary size may be seen to open directly into them (Fig. XIV). Whenever these vessels are present it is found that they are the only part of the vascular bed of the nodule which can be filled by an injection technique.

Histological examination of nodules containing these giant vessels shows that there is little thyroid parenchyma surrounding the dilated vessels. Only a few vesicles are seen and usually there is a large amount of the pale-staining material, often referred to as extra-vesicular colloid, in these nodules.

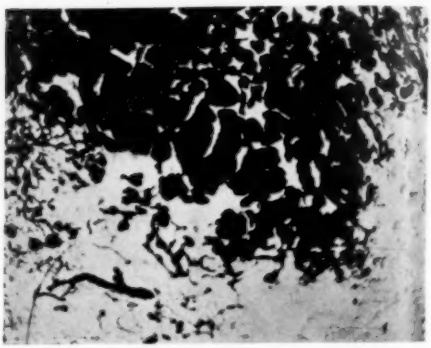

FIG. XIII. Photomicrograph of a section of injected nodular goitre. Many giant sinusoidal vessels are clearly seen. Their size may be judged by comparison with the capillaries seen in the lower part of the photograph. (x 25)

Now when either change is present in the nodular vessels of the perfused gland it acts as an arterio-venous shunt. Arterial perfusion results in venous filling and when the gland is examined, it is seen that only the giant vessels or the dilated hyperplastic vessels show the presence of the injection medium (Fig. VI).

Haemorrhage and necrosis in thyroid nodules

Haemorrhage, necrosis and cyst formation are changes which are frequently observed in thyroid nodules (King, 1952). Clearly the occurrence of these processes will greatly modify the vascular pattern within a thyroid nodule. In only one case in these experiments was the plane of section fortunate enough to provide a clear display of the vascular bed in the necrotic nodule (Fig. XV). It can be seen in this specimen that most of the thyroid lobule is replaced by

necrotic debris. However, in one quadrant the stump of the original arterial tree remains unchanged. Under a higher magnification (Fig. XVI) the details of this vascular tree may be made out. Joining the tips of its branches are capillary loops, the general pattern resembling that seen in granulation tissue. In the base of the "tree" remnants of vascular pattern in the capillary bed may be clearly observed.

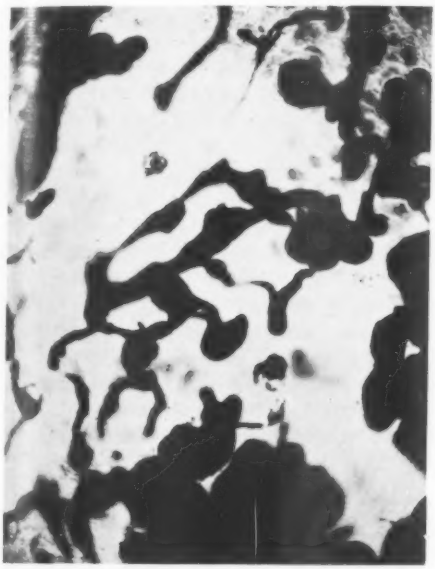

FIG. XIV. Photomicrograph of a section of injected nodular thyroid gland showing some giant vessels in greater detail. The variation in calibre is well seen and vessels of capillary size can be observed opening directly into the giant vessels. (x 100)

DISCUSSION

It has been pointed out that the thyroid nodule is essentially an enlarged thyroid lobule and that it is supplied by the lobular artery. A similar type of change is well recognized in such tissues as breast and uterus. In these organs local masses of hyperplastic tissue are found and they can often be shelled out of the surrounding tissue, being attached at one point, their hilum, through which their blood supply enters. The various changes which may be observed both in and around the nodules have been discussed. Terry and Delamere (1924) have investigated the blood supply of a series of nodules removed surgically. They concluded that the nodule received its blood supply from many vessels which joined it from the capsular plexus. However, in two of their published illustrations they show a nodule supplied by a single large vessel and a few small vessels which run across the capsular space. This is what is to be expected when larger nodules are investigated: the nodules they describe were large enough to warrant surgical excision. Moreover they describe degenerative changes in most of their nodules and these degenerations are particularly liable to distort the original vascular pattern of the nodule.

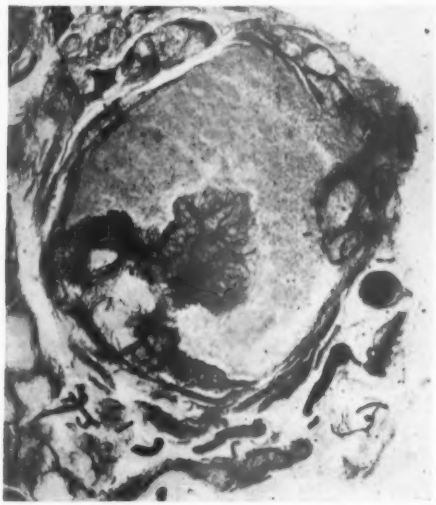

FIG. XV. Photomicrograph of a section of an injected nodular goitre. The residual vascular bed in a necrotic nodule is to be observed. (x 10)

In the technique used in these experiments a period of eighteen hours is allowed to pass before the glands are injected, thus giving time for any post-mortem spasm of the smooth muscle in the vessel wall to pass off. This means that in the perfused gland there is absolutely no vasomotor tone or control.

The path taken by the perfusing medium in such circumstances will clearly be determined by relatively straightforward hydrodynamic factors, depending on such variables

as pressure of perfusion, length and diameter of the vessels and their pattern of branching. Now under such conditions it is observed that, whereas a normal gland will show complete capillary bed-filling on perfusion, the nodular gland is characterized by patchy filling within the nodule (Fig. VI). This has been a constant finding and, throughout the series of experiments, no case of complete and uniform filling of the vascular bed of the nodule was observed.

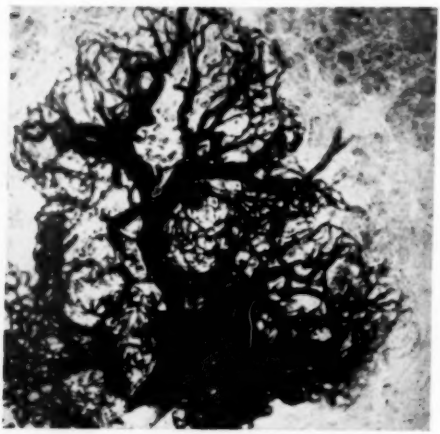

FIG. XVI. Photomicrograph of a section of the injected nodular goitre shown in Fig. XV; it shows the remaining vascular tree in greater detail. (x 50)

Moreover, if there should be the development of either a hyperplastic area within the nodule or of giant vessels (those having never been observed in a normal gland), such areas are found during injection to act as intranodular arterio-venous shunts. When this occurs, arterial perfusion results in venous filling and continued perfusion merely results in the medium running through the nodules and out into the veins. When nodules such as these are sectioned it is found that no perfusion medium has entered the general capillary bed of the nodule, all the fluid having been shunted through the altered vessels.

Now clearly, during life, all the tissues within the nodule must have a blood supply and it would seem reasonable to postulate some degree of vasomotor control as the factor which determines flow of blood through areas other than those which act as arterio-venous shunts. Furthermore, there is some evidence for the presence of arterio-venous shunts in the normal gland, these being situated between branches of the smaller arteries and veins. These also must surely be under the control of the vasomotor centre.

A further point deserves mention. Perfusion of the normal gland via the arteries shows that these vessels are possessed of considerable strength. The routine perfusion pressure in these experiments was 200 mm. Hg. and no case of extravasation of perfusion medium into the normal gland was seen. Even on raising the pressure to over 300 mm. Hg., no arterial rupture could be produced in normal glands.

However, if the gland were perfused via the veins, rupture of vein and extravasation occurred at pressures ranging from 80-90 mm. Hg. The range of figures is essentially the same as those recorded by Terry (1922) who postulated that haemorrhage into the thyroid gland and, in particular, into thyroid nodules was due to such factors as coughing and straining which, by raising the venous pressure, gave rise to rupture of the vein walls within the gland.

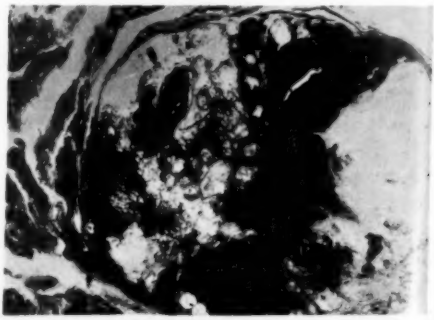

FIG. XVII. Photomicrograph of a section of an injected nodular goitre. This shows a single nodule in an otherwise normal gland. Note that whilst the normal gland is uniformly filled, the nodule shows patchy filling and extravasation of medium into the connective tissues. (x 12)

Now on perfusing nodular glands via the arteries at pressures of 200 mm. Hg., extravasation of medium into nodules was of frequent occurrence (Fig. XVII). The medium

was found both inside the vesicles and in the connective tissue spaces of the nodule, that is to say, the distribution is essentially the same as can be found when blood is extravasated into the thyroid. It has already been pointed out that various changes in the nodular vessels give rise to arterio-venous shunts in the perfused gland and it may be that both extravasation of medium into the perfused nodule, and of blood in the living organ is related to these arterio-venous shunts in that they allow fluid at high pressure through into the veins.

Turning now to the problems of haemorrhage and necrosis in thyroid nodules, it has been shown that the vascular supply to a thyroid nodule depends not only on local vessel pattern but also on vasomotor tone. It is well known that variations in both local and general vasomotor tone occur under a variety of conditions. In thyroid nodules variations in vasomotor control could give rise to the following possibilities:—

(a) There may be a pre-nodular arterio-venous shunt which, when functioning, could divert a large amount of the arterial inflow directly into a vein and away from the nodule, or when completely closed could increase the blood-flow through the nodule.

(b) Arterio-venous shunts within the nodule may determine the temporary cessation of blood-flow through a section of the nodule.

(c) Intra-nodular arterio-venous shunts may, by raising the pressure in the nodular veins, give rise to extravasation of blood into the nodule.

Furthermore, the vessels within the nodule, like those elsewhere in the body, may show various changes in their walls and rupture or thrombosis may result. However, as has been pointed out by King (1952), haemorrhage and necrosis in the thyroid nodules frequently occur in young people in whom there is no suggestion of arterial disease, and it is therefore suggested that physiological factors which give rise to alteration in blood distribution within the nodule are of more importance than organic changes in the vessels.

Changes in vasomotor control and vascular accidents would be expected to give sudden changes in the blood supply to various parts of the nodule. Observations indicate that more gradual changes also occur. It has been shown that the development of a hyperplastic area within a nodule gives rise to the development of many new vessels around that hyperplastic area, and these vascular areas may, by deviating blood away from the rest of the nodular parenchyma, result in a progressive atrophy of these tissues until ultimately necrosis and cyst formation may occur.

SUMMARY

1. An investigation into the vascular architecture of the nodular goitre has been carried out.

2. It is demonstrated that the nodule is essentially an enlarged thyroid lobule.

3. The blood supply to the nodule is clearly the enlarged lobular artery.

4. As the nodule forms, there develops a series of new vessels in its substance. These are termed nodular vessels and it is pointed out that they fall far short of any attempt to reproduce the vascular pattern of the adult gland. New lobules within the nodule do not occur.

5. The changes in the vessels surrounding the nodule are described. Initially these changes are merely those associated with disappearance of thyroid tissue. Should various changes occur in the nodule new vessels may appear, running between the capsule and the nodule.

6. The development of giant vessels and tortuous sinusoidal vessels is described within the nodule. When they occur they act, in the perfused gland, as arterio-venous shunts.

7. The significance of these findings with respect to the development of haemorrhage and necrosis within the thyroid nodule is discussed.

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THE TENDONS ON THE DORSUM OF THE HAND*

By D. R. Leslie

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The Extensor Tendons on the Dorsum of the Hand

Random observations in the dissecting room prompted a systematic study of the arrangement of the extensor tendons as they lie on the back of the hand in their course from the wrist to the fingers. The results of this investigation on 127 dissecting room hands are set out below.

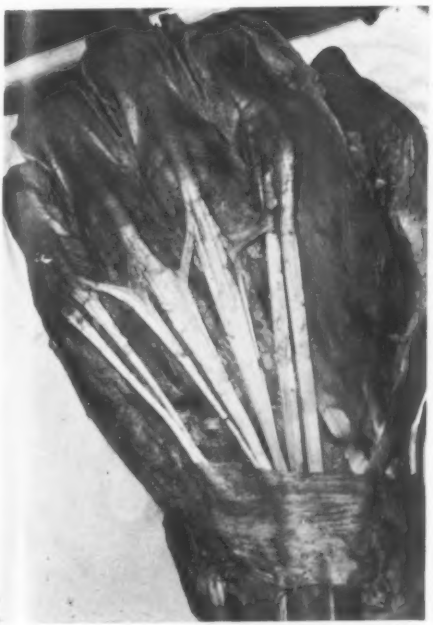

FIG. Ia. The extensor tendons on the dorsum of the hand showing the communicating slips, the double tendon of extensor digiti quinti and the relation of extensor indicis to extensor digitorum communis.

FIG. Ib. The communicating slips have been elevated on markers. Note that the slip from the little finger tendon to ring finger is larger than the continuation of the little finger tendon.

A. *Extensor digitorum communis*

The arrangement of the tendons of the extensor digitorum communis is more uniform than is generally described. The tendons radiating to the fingers communicate with each other on the dorsum of the metacarpal bones in quite an orderly way. The pattern is followed accurately in the majority of cases and has only minor variations in the remainder.

The typical arrangement is seen in Fig. I. It will be noticed that the interlacing slips from the extensor communis tendons are arranged in accordance with the following two rules:—

1. Each communicating slip is given off by the more ulnar tendon and passes obliquely distally to join the more radial tendon and reach insertion with this.

* The subject of a lecturette given at the Royal Australasian College of Surgeons in September, 1952.

2. These slips become stronger and thicker as one dissects from the radial side of the hand towards the ulnar side.

In this pattern, the individual slips take on the following shapes:—

(a) The slip joining the tendons of the index and middle fingers is slender and thin and barely deviates the index tendon from its straight course. It is seldom absent.

(b) The slip joining the tendons of the middle and ring fingers is somewhat thicker, and it does, in fact, deflect the tendons slightly from their straight courses.

(c) The slip joining the tendon of the ring finger from that of the little finger is very thick; it is in fact thicker than the remaining fibres of extensor communis which reach their insertion in the little finger.

Because of the strength of this slip, the extensor communis tendon destined for the little finger is drawn towards the ring finger, and lies closely parallel with the ring finger tendon. It only leaves in the direction of the little finger after the slip has been given off.

The bundle of tendons on the back of the 4th metacarpal

In most cases there is a broad flat band of tendons lying on the dorsum of the 4th metacarpal which looks rather like a frayed ribbon. It consists of the communis tendons destined for the ring and little fingers and has the tendon to the middle finger lying close along its radial side. Distally, a diamond-shaped split forms in this band as the tendon for the little finger gradually leaves its fellow; this diamond is closed distally by the slip from the little finger tendon running back to reach its insertion with the ring finger tendon; this slip sometimes runs in 2 or 3 parallel bands.

B. *Extensor digiti minimi*

It is well known that the usual arrangement for the extensor digiti minimi proprius is in the form of a double tendon as it lies on the back of its metacarpal. Because of the deflection of the common extensor of the little finger towards the ring finger, it is a common mistake among students to name as this tendon, the radial of the two halves of extensor digiti minimi proprius. The true nature of the tendons is seen from the position which each occupies as it passes under the extensor retinaculum. All the extensor communis tendons lie bundled in a single compartment of the retinaculum over the distal end of the radius with the tendon of extensor indicis, which separates them from the bone. The tendons of extensor digiti minimi lie in a separate compartment over the dorsal surface of the distal radio-ulnar joint.

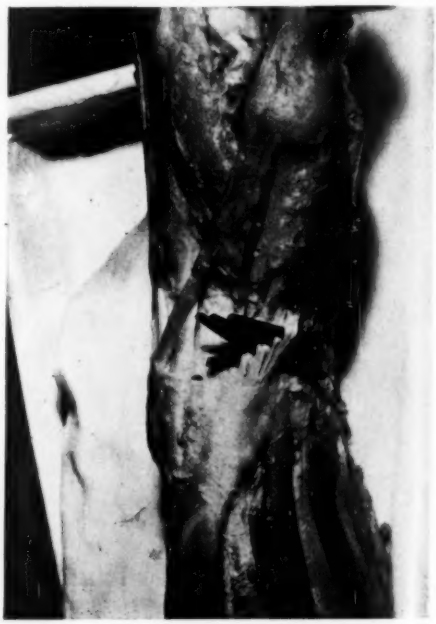

FIG. II. The area of the "anatomical snuff box." Note the thickness and multiple arrangement of the tendon of abductor pollicis longus.

C. *Abductor pollicis longus*

These observations have confirmed the well-known arrangement of the tendons of extensor pollicis brevis and abductor pollicis longus as they emerge from the extensor retinaculum on to the radial side of the

wr t. The tendon of extensor pollicis brevis is ways single and slender, whereas that of ab uctor pollicis longus is much stronger and is ways double or multiple, as in Fig. II.

FUNCTION

is obvious that the capacity for individual extension movement of the ring fin er is impaired by the great strength of the slips which its own extensor communis ten on gives to the middle finger tendon and rec ives from the little finger tendon. This no mal condition in the ring finger has caused an occupational disability in pianists which has called for a special operation to relieve it (Batty-Smith, 1942).

The other fingers are not so limited. As the strength of the communicating slips is greater towards the ulnar side of the hand, so it is to be expected that independent movement is more efficient in the more radial fingers. However the little finger, like the index, has a proper extensor tendon, which ensures a good range of active extension whatever the position of the adjacent fingers.

In the hands which were studied, posture of the fingers was taken into account, and a record was kept of the degree of flexion in which each finger was fixed. It was found that the exact slope of the communicating slips varied with the relative flexion or extension of the adjacent fingers, but the principles laid down earlier were not affected by finger posture.

In the living hand of a thin person, it is possible to see the outline of the extensor communis tendons and the way in which they move and deflect each other by the pull of the communicating slips. It is seen that the tendon to the little finger is deflected from the straight line in all positions, but the index tendon is deflected only when the other fingers are strongly flexed while the index is held straight.

VARIATIONS

A. *Extensor digitorum communis*

In this study 127 hands have been examined, and the above arrangement for the extensor digitorum communis tendons are found in 112. In the remaining 15 hands the variations were as follows:—

1. In 12 the slip given off by the middle finger tendon to the index was thicker than usual, but never as big as the slip from ring to middle. In a few of the hands there was some deviation of the index tendon from its straight course by the medial pull of this slip. In all cases the slip passes superficial to the extensor indicis proprius tendon without joining it.
2. In 4 hands the slip from middle finger tendon to index finger tendon was absent.
3. In one case there were two separate slips given from the ring finger tendon to the middle finger tendon.
4. In 3 hands there were two separate tendons of extensor communis to the little finger, of which the ulnar one ran a straight course whereas the radial one ran the normal course, deflected towards the ring finger.

In no case was any slip found to run in the reverse direction, i.e., each slip arose from one tendon and passed distally and radially to insert with the tendon of the finger next towards the thumb.

B. *Special extensor tendons*

The following variations in the special extensors were found in these 127 hands:—

(a) Tendon of extensor digiti minimi single only—5 hands (two of them the right and left of same subject).

(b) Tendon of extensor digiti minimi triple—3 hands.

(c) Tendon of extensor indicis double—3 hands. In one of these the two slips approached the communis tendon from the same side; in the other two the radial of the two passed deep to the communis tendon and joined it from the radial side.

(d) An extra tendon was present from the extensor digiti minimi which joined the communis tendon of the ring finger—2 hands, the right and left of one subject.

(e) An extra tendon from the extensor indicis which joined the communis tendon of middle—2 hands, the right and left of one subject.

CONCLUSION

These observations have supported the orthodox descriptions of the arrangement of the tendons of the special extensors of index and little fingers and the tendons of the long muscles of the thumb.

However, with regard to the diverging tendons of extensor digitorum communis on the dorsum of the hand, the communicating slips which connect these together are regularly arranged in conformity with two simple rules, and the haphazard arrangement illustrated in most text books is misleading.

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A NEW OPERATION FOR MITRAL REGURGITATION

By JOHN HAYWARD
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WHEN new conceptions arise, confusion is often caused by the persistence of terminology based on past views. Mitral disease is no exception, and it is necessary at the outset to make perfectly clear what is meant in this paper by mitral regurgitation requiring surgical relief.

TERMINOLOGY

The normal mitral valve neither obstructs the onward flow of blood nor allows regurgitation, but rheumatic disease usually both narrows the valve opening and prevents its complete closure. The relative clinical importance of the stenosis and the regurgitation has always been difficult to assess, and on this subject there has been much uncertainty which modern work is rapidly clearing. Before valvotomies were done the damaged valves were only seen and felt at post-mortem. The pathologist, quite rightly from the pathological point of view, always reported mitral stenosis when the orifice would not admit two fingers. He had, and still has, no means of assessing regurgitation. Therefore in all his fatal cases the cardiologist received the report that his patient had suffered from mitral stenosis. As the morbid anatomist has the last word, his statements are liable to be accorded oracular force, and it is not surprising that it is very few years since some cardiologists regarded mitral regurgitation as unimportant.

In the last five years a very large number of mitral valves has been palpated during life and the regurgitant stream felt, and there is no longer any doubt about its importance in many cases. Physicians promptly accepted the challenge of the new information provided by surgeons. From their cases which had all been cheerfully labelled rheumatic cardiac with mitral stenosis they had to learn to sort out those requiring valvotomy, and numerous excellent papers on the clinical assessment of suitability for valvotomy have appeared.

There is still, however, a tendency to think of the cases of mitral disease as belonging to two groups—mitral stenosis suitable for valvotomy and mitral stenosis not suitable for valvotomy—and to regard regurgitation as something which occurs to a variable extent in mitral stenosis. While in theory this attitude is easily defensible, I believe that clinically, and still more from the practical surgical point of view, it is unsatisfactory. After all, it would be just as reasonable to regard all the cases as patients with mitral regurgitation with varying degrees of associated stenosis, and the special so-called mitral stenosis clinics set up recently in some hospitals could equally sensibly be called mitral regurgitation clinics.

The mitral orifice during ventricular diastole has to be narrowed to considerably less than two fingers before the obstruction to the flow of blood from the left auricle to the left ventricle is sufficient to produce symptoms. The regurgitant orifice during ventricular systole has likewise to be of moderate size before it assumes clinical importance. Though exact measurements cannot be given at present, it seems that an orifice just admitting one finger is about the critical size.

If a patient's mitral orifice during ventricular diastole is greater than one finger it is unlikely that stenosis plays much part in causing symptoms. It would be better not to label clinically such a case mitral stenosis, but to reserve this diagnosis for cases believed to have an orifice of less than one finger. Similarly a patient's mitral orifice during ventricular systole has to approach the size of one finger before regurgitation is likely to cause symptoms, and patients whose mitral valves leave a gap during ventricular systole equivalent in cross section to one finger or more are appropriately diagnosed as suffering from mitral regurgitation.

Accepting these criteria, and remembering that if the mitral cusps retain any movement at all the orifice will be smaller during ventricular systole, it follows that if the

orifice is small enough during ventricular diastole for the clinical diagnosis of mitral stenosis, it is not large enough for the clinical diagnosis of mitral regurgitation. Also if it is large enough for the clinical diagnosis of mitral regurgitation it is not small enough for the clinical diagnosis of mitral stenosis. The two are mutually exclusive. In other words, though patients with diseased mitral valves usually have both stenosis and regurgitation they seldom *suffer* from both, and the diagnosis should indicate which they are suffering from.

Borderline cases do occur in which the orifice is practically fixed at a size of approximately one finger. In these alone are both stenosis and regurgitation simultaneously clinically significant.

Details of clinical diagnosis are outside the scope of this paper, but I believe that on clinical grounds the vast majority of cases of mitral disease can be quite firmly provisionally diagnosed as suffering from mitral stenosis *or* mitral regurgitation, as the case may be. The former are suitable for valvotomy, and any regurgitant stream they have requires no treatment. The latter are not suitable for valvotomy because enlarging the mitral orifice which in them is already greater than one finger will produce little if any clinical improvment. For them a satisfactory operation is urgently needed which will close the orifice during ventricular systole, or at least narrow it to as much as possible less than one finger, without making it one finger size or less during ventricular diastole because this would merely substitute stenosis for regurgitation. Thus the adoption of the above terminology for clinical diagnosis has the paramount practical value that it makes the surgical requirements of each case immediately apparent. As will be seen below it also corresponds exactly with differences in the pathological anatomy of the diseased valve.

The operation to be described in this paper has been designed with the hope that it may help some of the patients who, following the above recommendation, would be diagnosed as suffering from mitral regurgitation.

PATHOLOGICAL ANATOMY

The problems in the surgery of the mitral valve are largely dependent on the pathological anatomy of the various types of deformity produced in the valve by rheumatic infection. A clear realization of the surgically significant differences in the deformities is essential to an understanding of the surgical requirements.

From the surgical point of view rheumatic infection affects the mitral valve in two main ways. The first is the development of fibrosis and contraction of the cusps and chordae tendineae, with or without calcification, and the second is fusion of the commissures. Up to a point both these effects can occur together, so that a valve with fused commissures may also have thickened, calcified and somewhat contracted cusps; but it is obvious that if the contraction of the cusps occurs to a degree which prevents the commissures from ever coming together they cannot fuse, and if fusion of the commissures has already occurred then the extent to which further fibrous contraction of the cusps can draw the valve margins apart is very limited.

Therefore, with the exception of a small group which I shall call intermediate, the majority of mitral valves affected by rheumatism fall into two distinct groups:—

Group I: Mitral disease with fused commissures

This is the valve of typical mitral stenosis with a "button hole" opening which will not admit the index finger (Fig. Ia). Obstruction to the onward flow of blood (stenosis) is the main cause of the circulatory trouble, and these cases are ideal for mitral valvotomy. The regurgitant stream can never be large because the valve opening is so small, and after valvotomy the cusps, being wide, will still come together during ventricular systole as well as if not better than before, so that any regurgitation which may be present makes a negligible contribution to the symptoms and requires no treatment.

Since this paper's main concern is mitral regurgitation no attempt is made here to subdivide this group.

Group II: Mitral disease with open or partly open commissures

This is the valve of typical mitral regurgitation with an opening which easily admits the index finger to the distal interphalangeal joint with room to spare (Fig. Ib, Ic). Regurgitation is the main cause of the circulatory trouble to which stenosis, if any, makes

a negligible contribution. These cases are not suitable for valvotomy. Even when the angle between the open commissures is partly filled in with dense fibrosis and calcification or one commissure is partly fused, as is often the case, splitting the fusion or incision in the angle with the valvotomy knife will do little good. Enlarging an orifice which is already large enough is unlikely to be beneficial and the tissue is usually too rigid to open and shut after division so that the hope that the cusps may be partly re-mobilized and the regurgitation thereby reduced is scarcely ever realized.

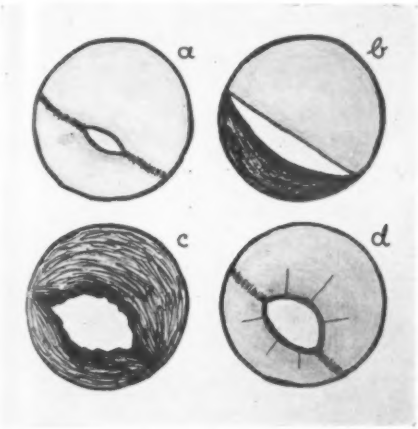

FIG. I. Diagrams of four types of rheumatic mitral valve. Each is imagined to be seen from the auricular aspect during ventricular systole, so that in each case the valve opening in the diagram represents the regurgitant orifice.

(a) Group I. Mitral stenosis. Both commissures fused.

(b) Group IIa. Mitral regurgitation. Posterior cusp thickened and contracted.

(c) Group IIb. Mitral regurgitation. Both cusps thickened and contracted.

(d) Intermediate Group. Conical valve. The lines radiating from the orifice are merely to suggest the conical shape.

This group may be further divided into two sub-groups:—

Group IIa: Function of posterior cusp permanently destroyed (Fig. Ib)

In this type of case the open commissures usually have little filling in or their angles and the aortic cusp is very nearly normal and quite mobile. The brunt of the damage has fallen on the posterior cusp which is thickened and contracted so that it can no longer move upwards and forwards to meet the aortic cusp during ventricular systole. A slit-like gap is left between the two cusps through which a flattened jet of blood regurgitates.

Group IIb: Function of both cusps permanently destroyed (Fig. Ic)

In this sub-group the damage to the valve is the most generalized and severe. Both cusps and the chordae tendineae are extensively thickened, contracted, and usually calcified. The angles between the open commissures are filled in to a considerable extent with rigid tissue. All movement of the valve is at a minimum. The end result is equivalent to a rigid irregular hole in a rigid wall, with total loss of valvular action. Blood swishes through it backwards and forwards with equal ease.

Intermediate Group: The conical or elastic valve (Fig. Id)

This is the type of valve in which stenosis and regurgitation may simultaneously be significant causes of circulatory trouble. There is both some fusion of the commissures and moderate thickening and contraction of the cusps. Calcification is usually minimal or absent. The valve opening feels elastic and is large enough to admit the index finger to the distal interphalangeal joint which it grips, and it continues to grip the finger as it is withdrawn. Digital pressure seldom splits the commissures which tend to push aside towards the ventricular wall and spring back when the pressure is relaxed. The chordae tendineae are shortened, and the fused commissures extend obliquely downwards from the atrio-ventricular ring towards the lumen of the left ventricle so that the opening is at the apex of a valvular cone. This is in contrast to cases in Group I in which the fused commissures and the button-hole orifice between them combine to form a tight band which stretches much more nearly straight across from side to side of the atrio-ventricular ring with the bodies of the cusps, if still mobile, billowing up on either side of it.

When the orifice of a conical valve is merely dilated no harm is done, but very little clinical improvement may be achieved. When the commissures are divided there is less stenosis but regurgitation may be increased, presumably because the freed cusps

are able to retract further apart, and the patient may be worse. Therefore, in spite of the presence of some fusion of the commissures, valvotomy results in cases with conical valves are liable to be disappointing.

Holmes Sellors and his colleagues (1953), discussing the anatomy of mitral stenosis, describe a type which they call Type III with fused funnel shaped thickened cusps. They picture it with a typical button-hole orifice. I have never met a case of this type. When the chordae are sufficiently contracted to draw the cusps into a conical or funnel shape I have always found that the orifice would admit one finger, and it seems likely that when the edges of the cusps are drawn well downwards by the shortened chordae the orifice will usually be of this size. To have a smaller orifice either the cusps would have to be widened, and this seems an unlikely result of the pathological process, or the atrio-ventricular ring very much narrowed.

Though most cases do fall reasonably easily into one or other of the above groups, it is not suggested that the classification of the anatomy of the rheumatic mitral valve given here should be regarded as rigid or final. Up to the present relatively few mitral valves in patients suffering from mitral regurgitation have been felt, because surgeons have usually only palpated them on the occasions when they were mistakenly regarded as mitral stenosis and submitted for valvotomy. It is very likely that a much better classification will be possible when more have been felt, but in the meantime the classification given here provides a preliminary working basis for the planning of operations for mitral regurgitation.

Principles Underlying the Surgical Treatment of Mitral Regurgitation

Once the anatomy of regurgitant mitral valves is understood, the surgical needs are easy to see. In cases with valves belonging to Group IIa the posterior cusp is too thickened to be of any further use as a moving valve flap, but the aortic cusp is either freely mobile or can be made so by a little freeing of its angles. Its movement will provide a sufficient range of opening and shutting of the orifice for an adequate circulation, so there is no need to attempt to produce an artificial movable posterior cusp. The significant mechanical fault is the fai ure of the posterior cusp to meet the aortic cusp during ventricular systole, and all tha is needed to make the valve reasonably effic ent is something attached over the posterior cusp to fill the regurgitant slit.

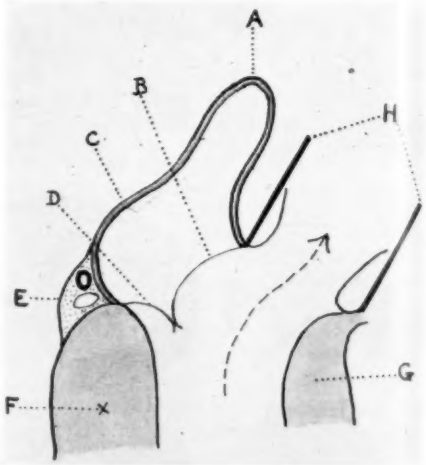

FIG. IIa. Diagram of a section of the heart through the middle of the mitral and aortic valves, seen from behind, below and medially. The line of section is indicated by the dotted line XY in Fig VI. This drawing, though much simplified, has been made from a normal heart fixed in formalin, so that the relative positions of the main structures are shown as accurately as possible. It is the prototype of the remaining diagrams in Fig. II and in Fig. V. In this diagram the mitral valve is normal and closed during ventricular systole. The papillary muscle masses do not appear in the section because it passes between them. The chordae tendineae are therefore omitted.

A. Upper part of base of left auricular appendage.
B. Aortic cusp of mitral valve.
C. Left atrium.
D. Posterior cusp of mitral valve.
E. Coronary sulcus fat containing circumflex branch of left coronary artery and coronary sinus.
F. Left ventricular wall.
G. Interventricular septum.
H. Aorta with its valve open.

In cases belonging to Group IIb the p ob-lem is more difficult, because both cusps ave permanently lost their mobility and any f ced tissue or foreign body placed in the r gid orifice would merely increase the stenosi to an extent equivalent to the reduction in re-gurgitation. The problem will only be so ved when something with mobility and valv lar

action is devised to fill the orifice during ventricular systole and retract out of the way during ventricular diastole.

In many parts of the world strips of pericardium, plastic substances and other devices are being tried to relieve mitral regurgitation by attempting to produce either a solid buttress over the edge of or just under the posterior cusp, or a movable structure with valvular action below the orifice. For various reasons none has so far proved satisfactory. As far as is known to the author, no one has previously tried using the auricular appendage, and this is what is suggested here.

THE NEW OPERATION

In this operation the left auricular appendage is invaginated through the mitral valve orifice and attached to the left ventricular wall under the posterior cusp. It is suitable for cases belonging to Group IIa.

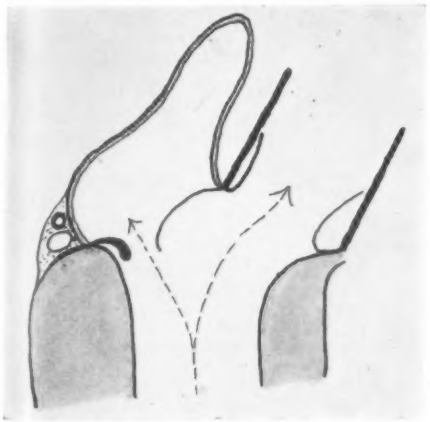

FIG. IIb. Diagram of the same section, but showing Group IIa mitral regurgitation. The posterior cusp is thickened and contracted. The aortic cusp is normal.

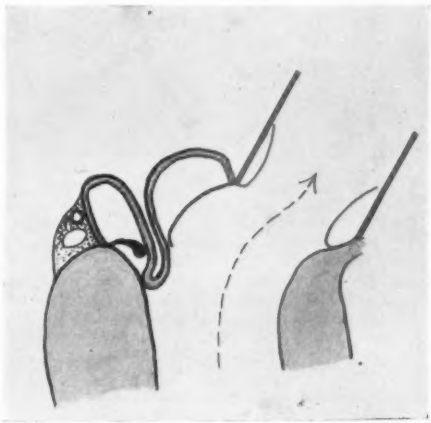

FIG. IIc. Same as Fig IIb, but with the auricular appendage invaginated to fill the regurgitant slit.

Trials on normal hearts in the post-mortem room showed that, despite the wide individual variation in the shape and size of the left auricular appendage, it was nearly always possible to turn it inside out and fix it in the new position, though it was usually not wide enough to reach from angle to angle of the commissures. As the appendage is almost invariably considerably enlarged in mitral regurgitation it was thought unlikely that there would be any difficulty in making it reach in these cases, and that it would probably be wide enough to extend from end to end of the slit between the cusps. The result would be a double thickness of appendage wall fixed against the edge of the posterior cusp (Fig. II). If this proved insufficiently thick to fill the regurgitant slit it could be made wider by putting folded pericardium or muscle inside the invaginated appendage. This operation was performed in the following cases.

Case 1

Mrs. J.G., a 38-year-old married woman without children, had rheumatic fever at the ages of 7, 12 and 25 years. Her heart was known to have been affected but she suffered from no circulatory disability whatever until five months before operation when, after a three weeks course of slimming tablets containing thyroid extract, her heart action suddenly became irregular and she was almost completely incapacitated. She was found to have auricular fibrillation and an attempt to restore normal rhythm with quinidine failed. Even after the fibrillation was well controlled with digitalis she was left with considerable disability. Shopping and housework were extremely difficult to manage, and she could only walk up five steps without stopping for breath. After coming up the ten low steps to her house she had to sit down for five minutes. As well as dyspnoea there was substernal pain, and she could not lie on the left side because this position brought on a choking feeling which spread up to the neck. She had only had one attack of nocturnal dyspnoea. There had been no congestive cardiac failure, no haemoptyses and no emboli.

The heart was not much enlarged, the apex beat was left ventricular in quality, the mitral first sound was absent with a relatively low pitched systolic murmur conducted well into the axilla. There was no opening snap, and only a short soft early diastolic murmur. The electrocardiogram showed no axis deviation, and on screening there was moderate systolic expansion of the left auricle. The left auricular appendage was large (Fig. III). The pulmonary second sound was accentuated and there were no basal murmurs.

marked, had almost vanished, and she stated that she felt better and could now lie on her left side without discomfort. Three weeks after the operation she walked up and down 24 stairs at a moderate pace without any discomfort and with no change in her respiratory rate.

Post-operatively a faint mitral first sound was present, the systolic murmur was higher pitched and "thinner" in quality, and the diastolic murmur was still soft, short, and difficult to hear.

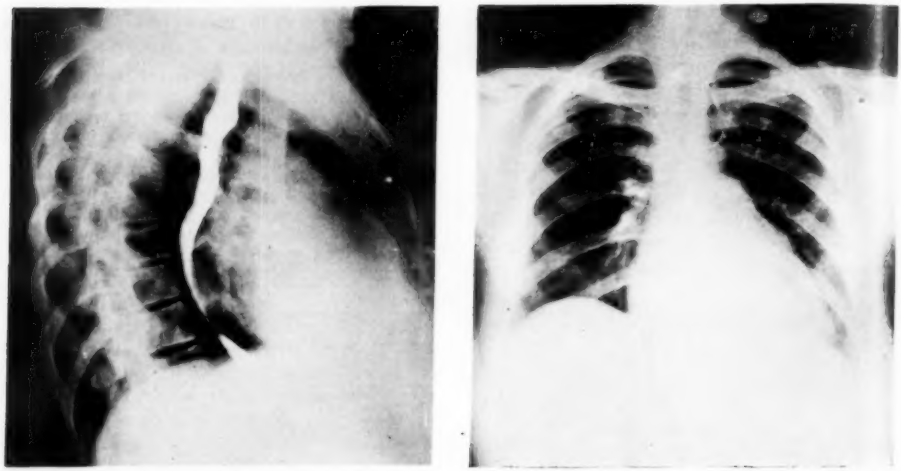

FIG. III. Pre-operative radiographs in Case 1.

At operation on 9th December, 1953, there was no clot in the auricle and her mitral valve was found to be typical of Group IIa. The commissures were open, the aortic cusp mobile, and the posterior cusp thickened, contracted and almost immobile. There was a powerful regurgitant jet. The exploring finger was withdrawn and the incision in the appendage closed. Then the appendage was pulled inside out through the valve and attached to the ventricular wall below the posterior cusp with a 6 lb. nylon stitch. The heart's action was very little disturbed by this manœuvre. The systolic thrill previously palpable in the left atrium was much less obvious, and examination with a finger in the invaginated appendage to a level just above the aortic cusp suggested that the edge of this cusp touched it during ventricular systole. It was decided that placing something in the invaginated appendage to make it wider was probably not necessary in this patient, and it was also thought wise to make this first trial of the operation as simple as possible. Interrupted stitches were put across the base of the invagination as an added insurance against it blowing right way out again.

The patient made an uninterrupted recovery no different from that after a successful valvotomy. Within two weeks her mitral facies, previously well

Case 2

Miss T.K., aged 38, had rheumatic fever four times, at the ages of 11, 15, 16 and 22. She only worked for six months at the age of 15 until her second attack of rheumatic fever. From that time she has required the invalid pension for her cardiac disability. She could not dance or hurry and needed two pillows, and subsequently her exercise tolerance has gradually declined. Since the age of 24 her heart has been fibrillating, and she has been on digitalis, and since the age of 33 (five years ago) she has required regular injections of diuretics. At this time she developed secondary tricuspid incompetence. For seven years midline interscapular pain as well as dyspnoea has occurred on exertion. She can walk up to about 100 yards very slowly, but she spends most of the day sitting in a chair. For many years she has not been able to go shopping and has slept with a back rest.

There have been no attacks of paroxysmal nocturnal dyspnoea, no haemoptyses and no embolic phenomena. She suffers from "bronchitis" every winter.

She was admitted on 28th December, 1953, emaciated and cyanotic. She had been like this for years. Her whole thorax and abdomen shook with

every heart beat, and there was visible systolic expansion of the liver and the veins in the neck to the angle of the jaw. The heart was huge and there was a systolic thrill palpable all over the front of the chest and maximal at the apex. A diastolic thrill was palpable only at the mitral area. A loud systolic murmur was audible everywhere in the chest and even in the neck, but a diastolic murmur was heard only at the apex in the sixth intercostal space four inches from the midsternal line where the apex beat was vigorous and heaving. With slow heart beats only the to and fro systolic and diastolic murmurs could be heard at the apex, but with rapid beats there was a slapping first sound. The pulmonary second sound was accentuated and widely split. There were no moist sounds in the lungs. The blood pressure was approximately 170/100 mm. of mercury.

Films of the chest showed a huge heart with a giant left auricle and only moderate pulmonary congestion (Fig. IV). Considerable systolic expansion of the left auricle was seen on screening.

was a very large and extremely powerful regurgitant jet, and during ventricular systole the left auricle felt as hard as the ventricle. Its wall was about two millimetres thick and very tough. The lateral commissure was wide open but the medial commissure was partly fused at its angle. This was easily split and there was then excellent movement of the aortic cusp. The appendage was invaginated, with difficulty because of the huge intra-auricular pressure to work against, and fixed below the small contracted posterior cusp. A piece of chest wall muscle was pushed into it before its base was closed. It then seemed to make reasonable contact with the aortic cusp during ventricular systole and the systolic expansion and thrill in the left atrium were less.

Her post-operative course was complicated by transient weakness in the right hand and very slight nominal aphasia which was first noticed on the third day and was gone by the third week. There was also moderate pyrexia up to about 102°F for two weeks, for no obvious reason. Otherwise, up to the

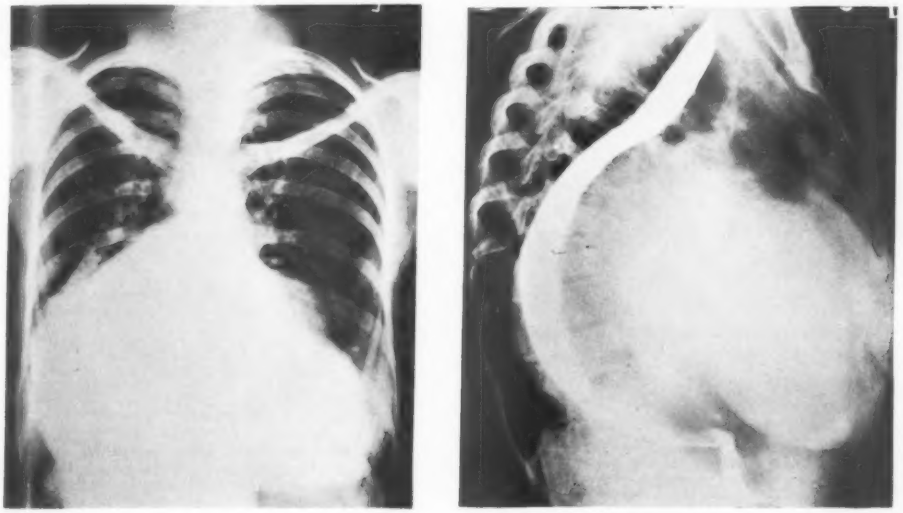

FIG. IV. Pre-operative radiographs in Case 2.

She was regarded as a case of gross mitral regurgitation with secondary tricuspid regurgitation, and she was chosen as the second case for trial of the new operation because it was felt that if the operation could improve such an advanced case it must be of some use. The seriousness and the experimental nature of the procedure was explained to her, and it is a tribute to her great courage that she agreed to the operation.

At operation on 7th January, 1954, the pericardium was found to be generally adherent, there were no clots in the auricle, and the mitral valve belonged to Group IIa. There was no calcification. There

present time (three weeks after operation), her progress has been satisfactory. The heart's action has become quieter, the systolic pulsation in the neck veins and in the liver has almost gone, the cyanosis has gone from her finger tips, and she can sleep lying flat and prefers this position. Her heart rate is now controlled with 0.25 mgrms. of digoxin per day, namely half the pre-operative dose, and she has required no diuretic injections for the past ten days. She can walk up and down eight steps without difficulty, and would have been willing to go further if she had been allowed. Her systolic murmur and thrill are much less forceful. The diastolic murmur and thrill seem unchanged.

A modification of this operation has been designed for cases belonging to Group IIb, in which a moving part with valvular action is required in the mitral orifice. If, instead of the whole left auricular appendage being turned inside out and part of its free edge fixed to the ventricular wall, part of it, a short distance from the tip on its outer wall, could be so fixed, the result would be invagination of all except the tip. The tip would remain right side out as a conical projection like a paper hat inside the invaginated part, fixed to the ventricular wall along its lower outer margin. During ventricular diastole it should remain flattened and empty causing minimal obstruction to the flow of blood from the left auricle to the left ventricle. During ventricular systole it should balloon with blood and its inner part should make contact with the aortic cusp and close the orifice (Fig. V).

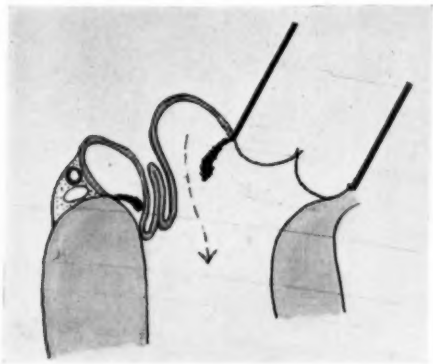

FIG. Va. Group IIb mitral regurgitation. Both cusps thickened, contracted and fixed. Imaginary diagram of how incomplete invagination of the auricular appendage should look during ventricular diastole.

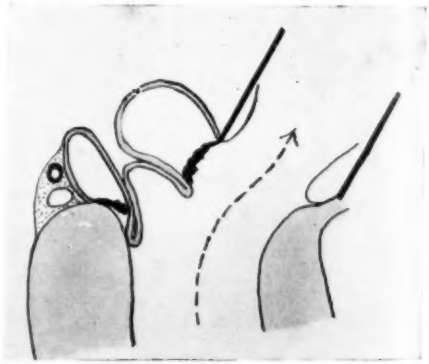

FIG. Vb. The same during ventricular systole. The uninvaginated tip of the appendage is imagined to have filled with blood and closed the mitral orifice.

This operation has not been attempted because the two cases which have been done did not require it, and I am not certain if it will ever be possible or, if possible, that it will work. In neither of the cases described would the appendage have been long enough, and it may never be. I only mention this untried idea because I cannot yet advise with certainty how to differentiate sub-groups a and b of Group II cases clinically and, for the time being at least, any surgeon operating for the relief of mitral regurgitation may expect to encounter some cases in which the aortic cusp is rigid and cannot be sufficiently mobilized. He should therefore have some plan of what he hopes to do in such a case.

It has been pointed out that cases in the Intermediate Group suffer from both stenosis and regurgitation and that the result of valvotomy in them is often disappointing. Perhaps they should have both valvotomy and invagination of the auricular appendage, but as this has not yet been done nothing further can be said about it.

TECHNICAL DETAILS OF THE OPERATION

Several technical points require further description and discussion.

The mitral valve is first explored with the finger through the left auricular appendage exactly as in the operation for mitral valvotomy. The type of valve defect is diagnosed, and, if any improvement in the mobility of the aortic cusp can be achieved by freeing or cutting the angles of the commissures, this is done. The position of the commissural angles in relation to coronary arterial branches on the surface of the left ventricle is noted carefully and the subsequent position of the invaginating stitch or stitches planned in relation to them. Then the finger is withdrawn and the appendage closed with mattress or continuous stitches

or both. A purse-string stitch is not used, or, if used, should not be tied because the aim is to deform the appendage and interfere with its blood supply as little as possible.

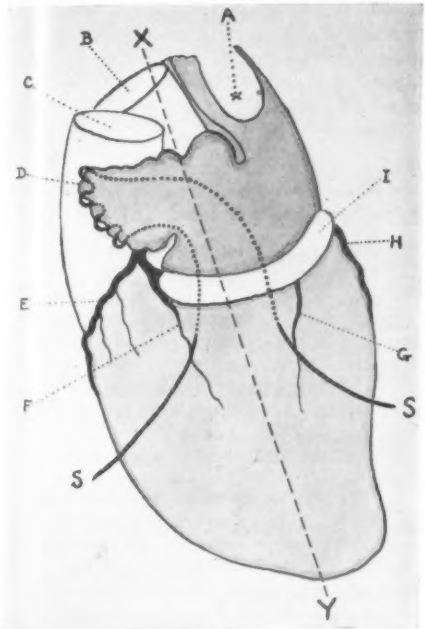

FIG. VI. Diagram of posterolateral aspect of the heart. This was drawn from a normal heart placed so as to give much the same view as the surgeon sees at posterolateral thoracotomy. The whole of the visible ventricular surface is left ventricle. Only the anatomical features of importance to this paper have been depicted. For instance no coronary veins are shown and only the upper parts of the descending branches of the coronary arteries are indicated.

A. Orifice of left inferior pulmonary vein, open at the top because in this specimen the top of the left atrium had been cut away.
B. Ascending aorta.
C. Pulmonary artery.
D. Left auricular appendage with invaginating stitch inserted along its margin from the tip downwards.
E. Anterior descending branch of left coronary artery.
F. Second descending branch of left coronary artery.
G. Third descending branch of left coronary artery.
H. Posterior descending branch of right coronary artery.
I. Coronary sulcus filled with coronary sinus and circumflex branch of coronary artery embedded in fat.
SS. Ends of the invaginating stitch emerging from the left ventricle between the second and third descending branches of the coronary artery.
XY. Line of section for the diagrams in Figs. II and V.

The appendage is then invaginated by means of 6 lb. braided nylon thread which is first inserted with a small needle as a running stitch along the edge of the appendage from its tip downwards for about two centimetres (Fig. VI). This length should be less than the distance between the angles of the commissures because when it is drawn down to the ventricular wall below the posterior cusp the part above it in the actual valve orifice will be wider. Both ends of the stitch are left long and a large ½ circle needle is threaded on to each end in turn and passed in through the appendage, through the valve orifice and out of the appropriate part of the ventricular wall. Finally the two ends of the stitch are tied over a piece of pericardium on the ventricular surface to stop them cutting into the muscle, while the assistant helps the invagination of the appendage by pushing it in with his finger.

The effect of the invagination is then assessed by palpating the surface of the atrium for any change in the systolic thrill, and the valve itself with the index finger inside the invagination. If it is found that the appendage does not reach satisfactorily into one or other commissure another mattress stitch can be inserted from above down the invagination and out through the ventricular wall to correct this defect. If the posterior cusp is not adequately buttressed a suitable amount of folded pericardium or muscle from the chest wall can be inserted down the invagination. Then the base of the invagination is closed by placing a few interrupted stitches across it.

The positions at which the two ends of the invaginating stitch emerge on the ventricular wall is important. Before it finally anastomoses with the right coronary artery where the latter terminates in its posterior descending branch, the circumflex branch of the left coronary artery usually gives off two unnamed descending branches of moderate size which pass down the surface of the left ventricle (Fig. VI). For convenience I shall call them the second and third descending branches so that the four descending branches supplying the left ventricle in order from front to back are the anterior, the second, the third and the posterior descending branches. The anterior and posterior descending

branches of course also supply the right ventricle. There are usually other very tiny descending branches.

Though the extra descending branches of moderate size are nearly always two in number they are unfortunately rather variable in position and their associated veins are not always close to them. Needless to say, they must not be included in the invaginating stitch. Usually the second descending branch arises in the coronary sulcus outside the atrio-ventricular ring nearly opposite the angle of the lateral commissure of the mitral valve inside, and the third descending branch likewise arises nearly opposite the angle of the medial commissure. This was the state of affairs in Case 1 so that the appendage could be invaginated satisfactorily with one stitch with its ends coming out of the ventricular wall between but close to each of these arteries (Fig. VI). When the stitch was tied no major coronary vessel was occluded.

Sometimes the two vessels arise closer together, and the second not infrequently has an oblique branch which crosses the space between them. Therefore more than one invaginating stitch will often be required. This was the state of affairs in Case 2 in which four invaginating stitches were used. It may be necessary to have one stitch between the two vessels and another in front of the second descending branch and possibly even a third behind the third rescending branch. Further experience will show whether this is ever the case.

It is considered important to use a rigid needle because only with such a needle has the surgeon reasonable control of the point and awareness of its position at all times. The malleable needles which have been designed for trans-ventricular stitches are unsatisfactory because the moment they enter the wall of the ventricle violent contractions of the ventricular muscle bend them and the surgeon has no precise control over where the point will emerge. I have used ordinary large $\frac{5}{8}$ circle needles with the points filed off and rounded so that if they touch the cusps when being directed through the mitral orifice they will slip off rather than stick into them. A needle of 8 cm. diameter was found satisfactory. In Case 1 it was found easy and safe with this rigid blunt needle to feel the way through the valve orifice without the assistance of a directing finger inside the heart, but in Case 2 with the huge heart it was more difficult to control the needle. Perhaps it would be better to pass the needle with the left hand while directing it with the right index finger in the auricle and through the valve. The auricle would then be closed after the invaginating stitches are passed and before they are tied.

DISCUSSION

Several important principles which underlie the operation are worthy of mention.

1. The invaginated auricular appendage is a living pedicled graft with its blood supply intact, or at least damaged as little as possible by the sutures and the incision for preliminary digital exploration.

2. The operation leaves nothing but living endocardium in contact with cardiac blood. The risk of post-operative intra-cardiac thrombosis should be at a minimum.

3. The tissue forming the heart valves, despite its unimpressive appearance under the microscope, is probably the most remarkable fibrous tissue in the body. Normally extremely thin and without blood vessels except at its attachment to the atrio-ventricular ring, it is yet able throughout life ceaselessly to withstand relatively enormous forces and friction. No material made by man nor any other tissue such as pericardium is ever likely to survive such continuous buffeting without wearing out, but there does seem a reasonable chance that living auricular wall, so closely related embryologically to the valve flaps, may have within it tissue capable of standing the racket of life within a cardiac valve.

4. In surgery in general, the simplest operation which is effective is always the best. This operation is relatively simple to perform and, except a large blunt needle, requires no special instruments other than those used for mitral valvotomy.

Against these advantages there are possible limitations.

1. The appendage may be too small for the operation to be possible. Fortunately in mitral regurgitation the appendage is usually large. It is not yet known in what proportion its size will be inadequate.

2. The appendage, and possibly the atrium also, may contain clot. This seems less common in mitral regurgitation than in mitral stenosis, possibly because in regurgitation there is much more turbulent movement of blood back and forth. The proportion of cases of mitral regurgitation which will be found to have intra-auricular clot is not yet known, nor in how many the clot may be removed first and then the appendage invaginated.

3. It is unlikely that the appendage will ever be made to fit the regurgitant space exactly, and the trabeculae on its inner wall do not present a smooth surface for contact with the aortic cusp, so that some regurgitation will always remain. However if the regurgitant space can be reduced in total cross section to considerably less than one finger the symptoms of mitral regurgitation should be largely relieved.

4. Late results are quite unknown. Only time can show what the fate of the invaginated appendage will be. All that can be said at present is that the immediate results in two cases are most encouraging.

No apology is offered for presenting such an early preliminary report when only two cases have been so recently done. The bitter disappointment and misery of patients with mitral disease whose hope for the future is killed by rejection for valvotomy because of regurgitation is sufficient reason for prompt publication so that, if any thoracic surgeons elsewhere see possible merit in the operation, they may make trials of it. It will then be rejected, modified or established in the shortest possible time.

Summary

1. It is suggested that most cases of mitral disease can be provisionally diagnosed as mitral stenosis or mitral regurgitation.

2. A classification for surgical purposes of the pathological anatomy of diseased mitral valves is given.

3. A new operation for correcting mitral regurgitation in which the left auricular appendage is invaginated through the mitral orifice is described and discussed, with a report of two successful cases.

Acknowledgements

It is a pleasure to acknowledge the information about the mitral valve given so freely to me by the many thoracic surgeons whom I visited early in 1952, especially Mr. R. C. Brock, Mr. T. Holmes Sellors, and Mr. W. P. Cleland of London, and Dr. Dwight E. Harken of Boston. I should also like to mention the stimulus to cardiac surgery in this country provided by the visits of Mr. W. P. Cleland late in 1952, and Dr. Frank Gerbode of San Francisco in August, 1953. For the successful outcome in the two cases I am deeply indebted to the anaesthetist, Dr. Margaret McClelland, to the expert assistance and care given by my resident medical officer, Dr. Kenneth Fairley, and to the nursing staff in the ward and operating theatre. I am also most grateful to Dr. June Howqua who was in charge of Case 1, and to Dr. Kenneth Grice who was in charge of Case 2, for their help and encouragement.

Addendum

At the time of correcting the proofs of this article, twelve weeks after the operation in Case 1 and nine weeks after Case 2, it is disappointing to report that both patients have deteriorated to a condition similar to, or perhaps slightly worse than, their preoperative state. In each case the retrogression began gradually about six weeks after the operation. It is probable, therefore, that the operation as described is unsatisfactory.

The reason for its failure is not known with certainty. It may be that the theoretical basis advanced for it is false, but the unmistakable initial improvement in both cases seems against this conclusion. Perhaps it is more likely that the auricular appendage has failed to become fixed in the new position because endocardium has not fused with endocardium, and that it has therefore gradually escaped from the sutures and retracted out of the valve orifice. Only post-mortem examination will show if this has occurred, and both patients are still alive. It is hoped that this paper, though now known to report failures, may yet be a small stepping stone on the difficult path to successful surgery for mitral regurgitation.

Reference

Holmes Sellors, T., Evan Bedford, D., and Somerville, Walter (1953), *Brit. Med. J.*, page 1059.

ACUTE STREPTOCOCCAL GANGRENE OF THE SKIN

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ALTHOUGH not common, acute streptococcal gangrene of the skin presents problems both of diagnosis and management, and the mortality rate remains high despite antibiotics and modern supportive therapy.

In 1883 Fournier (1883, 1884) reported a case of acute gangrene of the external genitalia in a female and although bacteriological confirmation is lacking, this may be the first published case of acute streptococcal gangrene. Further case reports appeared in the French literature, which has been reviewed by Bodin (1928) and Bate (1929). Fedden (1909) and Pfanner (1918) reported the first cases affecting the extremities, and Meleney (1924) recorded 20 further cases. Several cases of acute gangrene of the male genitalia have been recorded (Seeman, 1919; Hawkins, 1922; Campbell, 1922; Stirling, 1923). Acute streptococcal gangrene of the trunk is less common, although Lyle (1925) mentions that it was seen during the 1914-1918 war, and Fallon (1929) reported a case involving the breast.

After the classical papers of Meleney (1924, 1933), which clearly described the disease and differentiated it from gas-gangrene and erysipelas, case reports appeared with increasing frequency. These later reports have been reviewed by Meleney (1949).

The present paper reports two further cases of acute streptococcal gangrene, and reviews the pathogenesis and management of the disease. Yates (1953), reported a possible case from this country, although the clinical picture was not typical and bacteriological confirmation was lacking. The second case in the present paper is the first proven case of acute streptococcal gangrene reported in this country. In the first case reported here the diagnosis was made on the clinical picture alone.

Case Reports

Case 1

A male aged 41 years of age was admitted to hospital nine days after he had developed a small, painful blister in the left groin which he had pricked with a needle. This enlarged rapidly and on the third day gangrene appeared and a second lesion developed on the outer aspect of the left arm. Penicillin was administered for four days before he was referred to hospital.

On examination there was an oval ulcer three inches by four inches in the left inguinal region. The edge was irregular and undermined, and surrounded by a zone of black slough half an inch wide. The floor was covered with grey slough and yellow purulent material. There was oedema and the regional lymph nodes were enlarged and tender. A similar, smaller, lesion was present on the left arm. His general condition was satisfactory.

Immediate treatment consisted of penicillin (500,000 units six hourly), streptomycin (0.5 gram twelve hourly), and local Eusol dressings. Next day the ulcer was extending and his general condition had deteriorated. His temperature was 103 degrees F., pulse 130 per minute, respiration 40 per minute, blood pressure 80 mm. of mercury systolic, 60 mm. of mercury diastolic, haemoglobin 83 per cent. (12.2 grams) and white cell count 20,000 per cmm. Peripheral circulatory failure developed and intravenous therapy was begun, at first with blood transfusion and later saline infusion. The dose of penicillin was increased to 1,000,000 units three hourly. His condition did not improve. Paralytic ileus developed and a pericardial friction rub became audible for the first time forty-eight hours after admission. At this stage investigation of plasma electrolytes showed K^+ 5.0 milli-equivalents per litre, Cl^- 68 milli-equivalents per litre, and HCO_3^- 10 milli-equivalents per litre. An X-ray of his chest and examination of his cerebrospinal fluid were normal.

His general condition did not improve and the ulceration continued to spread. Six days after admission he developed auricular fibrillation and peripheral circulatory failure and died a few hours later.

Post-mortem examination revealed a fibrinous pericarditis and recent myocarditis with ecchymoses over the surface of the heart. Bronchopneumonic changes were present in the lower lobes of both lungs. The spleen was enlarged. There was no evidence of healing of the ulcer. Other organs were macroscopically normal.

Bacteriology: Repeated attempts to isolate any organisms from the ulcers or the blood stream, using both aerobic and anaerobic methods, were unsuccessful.

Case 2

A male aged 43 years was admitted to hospital forty-eight hours after he "strained" his shoulder attempting to stop a box falling from a trolley. Several hours later the shoulder became swollen and painful and he attended the family physician. Twenty-four hours before admission the skin over the area became reddened and swollen. Twelve hours later this erythematous area had extended over the left anterior chest wall and several small vesicles had appeared above the left nipple.

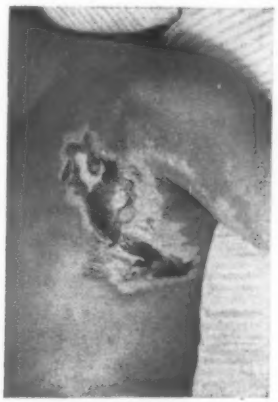

FIG. I. Acute streptococcal gangrene of the skin. This shows the condition of the local lesion (Case 2) on admission to hospital. There is a central slough with peripheral vesiculation and erythema.

Examination of the chest wall revealed a widespread non-tender erythema extending from the anterior aspect of the left shoulder over to the right axilla and from the left posterior triangle of the neck down below the nipples to the costal margin. Just above the left nipple there was an area of purplish vesiculation about three inches in diameter. General examination revealed temperature 102.4 degrees F, pulse 156 per minute, blood pressure 100 mm. of mercury systolic, 65 mm. of mercury diastolic.

Penicillin was begun immediately in a dosage of 1,000,000 units intramuscularly every three hours. Over the next six hours the area of erythema extended, the edge advancing by one inch. At this stage the patient's general condition suddenly deteriorated. He became mentally disorientated and developed peripheral circulatory failure, with blood pressure 70 mm. mercury systolic, 0 mm. mercury diastolic, profuse sweating and cold clammy extremities. Intravenous therapy was begun with one litre of normal saline followed by one pint of blood. One cubic centimetre of Eschatin was administered intravenously. Soluble sulphamezathine was given intravenously in a dose of one and a half grams six hourly. These measures resulted in an improvement in his general condition. Twenty hours after admission he was still extremely ill. Oliguria was present so that sulphamezathine was discontinued, being replaced by intravenous aureomycin (100 mgms. two hourly); persistent vomiting precluded oral therapy. The erythema and vesiculation were still extending and it was apparent that the chemotherapy was having little effect in controlling the spread of the infection. The patient became dehydrated with a haemoglobin of 118 per cent. and the rate of administration of intravenous fluids was increased.

Thirty-six hours after admission both the erythematous and gangrenous vesiculating zones were extending and his general condition remained poor.

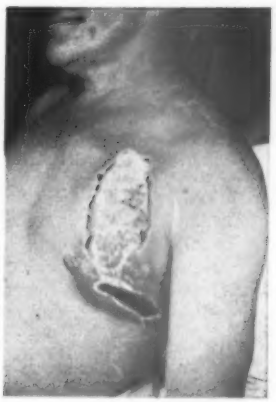

FIG. II. Same patient eight days later. The slough has separated leaving a clear granulating surface and the surrounding erythema has subsided.

The aureomycin was replaced by terramycin (500 mgms. six hourly) and magnamycin (300 mgms. six hourly) and the penicillin was increased to 2,000,000 units two hourly. Scarlet fever antitoxin (9,000 units) was also administered intramuscularly. Biochemical investigations showed total serum protein 4.8 grams per cent. (12 milli-equivalents per litre); albumin 3.5 grams per cent.; globulin 1.3 grams per cent.; serum chloride 68 milli-equivalents per litre; serum sodium 117 milli-equivalents per litre; serum potassium 3.7 milli-equivalents per litre; alkali reserve 10 milli-equivalents per litre. From here on the patient's general condition gradually improved and the erythema ceased to spread. It had reached the upper part of the left thigh and was meeting in the midline of the back. The large gangrenous patch in the region of the left nipple had localised. The patient was now icteric (serum bilirubin 2.5 mgm.).

A large slough was excised from the gangrenous area on the third day and thereafter smaller sloughs were removed as the occasion arose.

All antibiotic therapy was discontinued on the ninth day when the pyrexia had subsided. The patient was now eating well and sitting out of bed.

Four weeks after admission the granulating area was grafted with "postage stamp" size split skin grafts. There was a good take of this graft, although a second split skin graft was later necessary.

Bacteriology: On admission examination of vesicular fluid showed numerous streptococci in short chains. Cultures revealed β-haemolytic streptococci (group A), sensitive to penicillin, aureomycin and streptomycin, and haemolytic *Staphlococcus albus* sensitive to streptomycin and aureomycin. During convalescence secondary infection of the wound occurred with *Proteus vulgaris*.

His antistreptolysin titre was 1/400, indicative of recent infection with β-haemolytic streptococci.

DISCUSSION

The characteristic picture of acute streptococcal gangrene is well shown by these cases.

The onset may follow minor trauma such as an abrasion or injection, although in some cases no history of trauma can be obtained.

The initial lesion is a painful swelling with rapidly spreading oedema and erythema. The pain is often transitory and succeeded by numbness. Toxaemia is profound, often leading to prostration and peripheral circulatory failure. Vesiculation and gangrene appear from the second day onwards and may spread until the tenth day. At any time metastatic foci may develop.

Should the patient survive, demarcation of the slough appears after the first week and is usually complete in another week.

Since the mortality rate is from twenty per cent. to fifty per cent., energetic treatment is mandatory and early diagnosis essential.

The differential diagnosis is from gas gangrene, cutaneous diphtheria, erysipelas, anthrax, and the chronic gangrenes of the skin —progressive synergistic gangrene, gangrenous impetigo, fuso-spirochaetal infections and amoebiasis. It is discussed in detail by Meleney (1949).

Pathogenesis

The aetiological role of *Streptococcus haemolyticus*, first emphasised by Meleney (1924), is now generally accepted. The *Bacillus gangrenae cutis* of Nativille (1930) is probably a secondary invader of the *Proteus* group.

Streptococcus haemolyticus can be isolated in profusion from the central vesicles and gangrenous area, although it is absent from the spreading cellular oedema about the central area. If intensive antibiotic therapy is begun before cultures are taken, these may be sterile. The organism may be isolated from the blood in about twenty-five per cent. of cases in the acute stage. Later, secondary infection is almost invariable, the usual organisms being *Bacterium coli, Pseudomonas pyocyanea, Proteus vulgaris* and *staphylococci*.

There is no bacteriological or epidemiological evidence that a special stain of streptococcus is involved in this unusual clinical picture. It is probably a characteristic of the host rather than the parasite. It usually occurs in apparently healthy persons. Although Moore *et alii* (1950) reported two cases in diabetics, vascular disease is unusual. The metabolic defects producing skin gangrene in ulcerative colitis (Russell, 1950) are absent. Meleney has suggested that it may be a hypersensitive state of the Arthus or Schwartzmann type. On the other hand, Takahara (1952) has demonstrated an association between progressive oral gangrene and familial acatalasaemia. Further investigation is obviously necessary.

Antibiotic therapy

The antibiotic of choice is penicillin which must be given early and in high dosage. Because of the probability of secondary infection due to penicillin resistant organisms prevalent in all hospitals (Thomson, 1952), full and repeated bacteriological studies are necessary together with testing of any organisms isolated for antibiotic sensitivity.

Full doses of penicillin (1,000,000 units three hourly) and streptomycin (0.5 gram twelve hourly) are given, and further antibiotic therapy is guided by the patient's response and the response and the results of bacteriological studies.

In chronic skin gangrene Karn (1949) has reported good results with streptomycin while Meleney *et alii* (1950) state that bacitracin is dramatically efficacious.

Streptococcal antiserum

One patient (Case 2) was given streptococcal antiserum when there was no initial response to antibiotics. Fallon (1929) recommends its routine use. However Meleney (1930) reported a case of streptococcal gangrene at the site of the administration of scarlet fever antitoxin.

It is improbable that antisera have any place in the present management of acute gangrene of the skin, their role having been taken by antibiotic therapy.

Supportive therapy

In the early stages of acute streptococcal gangrene, peripheral circulatory failure is the chief threat to life. This occurred in both the present cases. Adequate supportive therapy is thus essential if the high mortality of this disease is to be reduced.

There is little precise information about the metabolic and circulatory upsets in this type of lesion. Electrolyte studies in the present cases were fragmentary but the results were similar in both cases. Both patients developed peripheral circulatory failure with hypotension, tachycardia, tachypnoea, sweating and cyanosis. There was gross depression of the serum electrolyte values of Na^+, Cl^-, HCO_3^- with hypoproteinaemia. One patient was icteric with hyperbilirubinaemia (2.5 mg. per cent.). Both were oliguric although neither became anuric. There was little change in plasma K^+ values.

In Case 2, fluid and electrolyte loss resulted in an initial elevation of haemoglobin to 118 per cent. (100 per cent. = 14.8 grams per cent.) with later anaemia (haemoglobin 75 per cent.) and concurrent icterus. This required blood transfusion. The first patient was anaemic (haemoglobin 83 per cent.) from the start of therapy. Autopsy in Case 1 showed acute myocarditis.

All this information suggests that the circulatory upset is due to a combination of three factors—direct "toxic" effects on the myocardium and peripheral vessels, extensive loss of fluid, electrolyte and protein into the gangrenous and erythematous areas, and haemolysis of erythrocytes.

This is somewhat similar to the picture seen in extensive burns. The area of the body surface involved in acute streptococcal gangrene may approach 50 per cent.

In the early stage of management intravenous therapy is necessary in all except the mildest cases. Blood transfusion is the treatment to be preferred, unless there is gross haemoconcentration when serum infusion is employed. Fluid must be given at a rate sufficient to maintain the blood pressure, and in amount sufficient to keep the haemoglobin between 90 per cent. and 105 per cent. At this stage careful observation of the patient is needed to prevent circulatory overloading. The pulse rate and blood pressure are recorded every fifteen minutes and the haemoglobin estimated hourly. The fluid balance must be charted accurately and a urinary output of at least one ounce hourly ensured. An in-dwelling catheter may be needed.

After the initial crisis, intravenous therapy is continued to make up the fluid and electrolyte lost, isotonic (0.9 per cent.) saline and 5 per cent. dextrose in water being used. As soon as possible the patient begins a diet rich in protein (120-150 grams daily), with vitamin and iron supplements. Repeated further transfusion of blood during convalescence may be necessary to overcome anaemia.

Adrenal cortical hormones

Neither adrenocorticotropic hormone (ACTH) nor cortisone were used in the management of the present cases, although Eschatin was given to Case 2 without definite result. No reports of the use of ACTH or cortisone in acute streptococcal gangrene have appeared in the literature.

Since these drugs may be life-saving in severe burns where the problems of resuscitation are not dissimilar, they may be of use in acute gangrene when there is no response to orthodox therapy. If the disease is in fact a hypersensitivity response, then treatment with ACTH or cortisone should give good results (Pickering, 1952). Noradrenalin may also be of value in the management of the circulatory failure.

Surgical management

The management of the local lesion is governed by the pathology of the condition. The lesion is essentially a necrosis of the subcutaneous fat with gangrene of the overlying skin, possibly due to thrombosis of the small blood vessels supplying it, (Meleney, 1933). Small pockets of pus may form under the edge of the ulcer after the major slough has separated.

If intensive chemotherapy is given sufficiently early in the disease surgical intervention may be unnecessary. Once the lesion has progressed to bullus formation or gangrene of the skin, most authors (Meleney, 1949) recommend excision of the slough which helps in relieving tension and permits free drainage of pus and oedema fluid thereby

reducing the extent of necrosis. The type of local application employed appears to matter little, although topical penicillin has been recommended. Areas of gangrene begin to demarcate towards the end of the first week. During the second week further sloughs may appear and further excision may be necessary. Any subcutaneous pockets of pus round the edge of the wound are adequately drained either by incision or by excision of the overlying skin.

If treatment is instituted early and the area of gangrene small, the wound may be permitted to heal by epithelial ingrowth from the edges. In most cases grafting is necessary and is performed as soon as conditions permit. Repeated cultures of the wound are made and chemotherapy adapted to the antibiotic sensitivities of the organisms isolated. Split skin grafts of "postage stamp" size are employed and occasionally pinch grafting is needed to complete skin coverage. Secondary foci are treated similarly to the primary lesion.

SUMMARY

1. The literature on acute streptococcal gangrene of the skin is reviewed and two further cases are presented.

2. The pathogenesis of the condition is discussed, and it is considered to be a hypersensitivity reaction of β-haemolytic streptococcal infection.

3. In management stress is laid upon intensive chemotherapy with close bacteriological control and adequate supportive therapy. The disorders of function producing circulatory failure in these patients are analyzed.

4. The surgical management of the necrotic lesion requires free drainage, excision of sloughs and later skin grafting.

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REPORT OF WORK WITH I^{131} AT THE ROYAL MELBOURNE HOSPITAL*

By R. Kaye Scott

Melbourne

Tracer Tests with I^{131} to Determine the State of Activity of the Thyroid Gland

Iodine is readily taken up by the thyroid gland. If radio-iodine is administered the kidneys, which excrete the iodide, and the thyroid are in competition for available supplies. The avidity of the pathological thyroid varies according to whether the gland is in a hypo- or hyper-functioning state. The amount of radio-iodine taken up by the thyroid or excreted by the kidneys can readily be measured, using Geiger-Müller counters, and uptake and excretion curves can be plotted.

But there are numerous complicating factors which make it difficult to find an easily determined test which will show some ratio between the dose administered and the proportion of that dose absorbed and metabolized by the thyroid. Such a test would be expected to yield a quantitative result by which hypo-thyroid, eu-thyroid or hyper-thyroid states could be distinguished and separated from each other. Many workers with iodine have applied themselves to this problem, and the literature contains numerous suggested indices. For example, there are the 24-hour thyroid I^{131} uptake of Werner, Quimby and Schmidt (1948, 1949); and Jaffe and Ottoman (1950); the accumulation gradient of Astwood and Stanley (1947); the thyroid clearance rate of Myant, Pochin and Goldie (1949, 1950); and several indices obtained from the amount of iodine excreted in a given time (Keating *et alii* [1947, 1949], Skanse [1948, 1949], Mason and Oliver [1949], Arnott *et alii* [1949]).

Radio-iodine was first available in Melbourne in 1948 (Scott, 1949) and Oddie (1949, 1950), then of the Commonwealth X-ray and Radium Laboratory, worked on an empirical scheme of iodine metabolism and determined a series of indices which could be obtained from thyroid uptake and renal excretion curves, which plotted the fate of the administered radio-iodine. At that time it was hoped that an arithmetic factor for thyroid output rate of metabolized Protein Bound Iodine could be obtained which would show whether the patient was in a hypo- or hyper-thyroid state.

These tests took almost a week to complete. The rate of thyroid uptake was indicated by the degree of acuteness of the initial slope of the uptake curve, and was called k_1; and the thyroid output factor, called k_4, was determined from the thyroid uptake curve and the renal excretion curve, after each had attained an equilibrium state, reached generally in the third and subsequent days after administration.

Mathematically, Oddie showed that the thyroid output rate factor k_4 was dependent on the uptake rate factor k_1. This would be expected because the uptake and output of the thyroid in a normal or pathological state would be in equilibrium provided that normal iodine in the diet remained constant in quantity.

The uptake factor k_1 could be determined on readings taken within the first 24 hours, and so it seemed unnecessary to persist with cumbersome urinary tests lasting over a period of nearly a week.

A second series of tracer tests was commenced late in 1950 and continued into the middle of 1952. The data obtained was used to compare our own indices with those proffered by overseas workers, and it was found that our k_1 was the most satisfactory of those tested for determination of the functional state of the thyroid.

However, careful plotting of the uptake curves was required and the subsequent deductions for determination of k_1 were not free from pitfalls because of the rapid rise of the uptake curve in the first hour, during

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which time only two counts could be made for plotting the initial part of the curve.

In July, 1952, Clarke of the Commonwealth X-ray and Radium Laboratory designed a new counting system. Twin counting chambers were used, one on each side of the neck, and the apparatus was set in position before the I^{131} was injected intravenously. The more sensitive instrumentation and the reduction of the survey time allowed the amount of the tracer dose to be reduced from 100 to 20 μ cs., while an initial determination of the amount of I^{131} in the thyroid could be obtained within the first few minutes after the injection. Ten or twelve plots could now be obtained within the first hour. The actual shape of the initial part of the uptake curve, which had previously been wrongly assumed to rise exponentially from zero, has now been determined. It has been shown from these investigations that an appreciable portion of the administered dose is absorbed by the gland from the blood within the first minute and that thereafter there is a progressive increase in the amount absorbed.

An index using the uptake curve obtained in a series of measurements taken during the first thirty minutes after injection is now being evaluated. Values for the index have been found which would appear to be in very reasonable agreement with the independently observed clinical, hypo-, hyper-, or eu-thyroid state of the patient, and these findings have been confirmed by Protein Bound Iodine estimations on the patient.

This new test which has been worked out by C. E. Eddy and K. H. Clarke has the advantage of simplicity of measurement and gives a reasonably reliable result within an hour or so of the administration of a minute dose or radioactive iodine. It should find widespread clinical application in the immediate future, but as with all indices which have so far been suggested it cannot always give a clear-cut result in a borderline case.

TREATMENT OF THYROTOXICOSIS WITH I^{131}

Radiation has a primary effect in causing suppression of cell secretions, and cases of thyrotoxicosis were treated with such enthusiasm by early radiotherapists that surgeons in general have not yet forgotten the skin damage that was caused. External radiation with modern techniques adapted to tissue tolerances will cause remissions in severely toxic cases.

Marine (1915, 1916) over twenty years ago showed that the thyroid has the capacity for concentrating iodine to an amount 4,000 times greater than that found in the serum. Immediately iodine had been prepared as an artificially radioactive substance it was used experimentally and therapeutically.

The isotope now in general use, I^{131}, emits beta and gamma rays. The beta rays have an average track in tissue of not more than 3 millimetres and these radiations yield 90 per cent. of the energy absorbed in the thyroid, the gamma rays with a much greater range of action contribute only 10 per cent. locally. If a test dose of I^{131} is administered and a section of biopsy material of the thyroid is placed on a photographic plate, the film is blackened over the sides of pick-up. The section may be stained *in situ* on the film and it is possible to compare histological structure with evidence of physiological function.

A normal thyroid so examined shows that only a minority of the follicles are active at any one time; some of the cells appear to be resting and so the pick-up is "spotty." The same findings are repeated in toxic glands.

With the limited range ot beta particles emitted by the I^{131} it is obvious that the resultant radiation effect will not be homogeneous. Increase of dosage may not necessarily accomplish the object. The radiation effect will only be increased locally, because average beta particle penetration will not be increased and outside follicles will be radiated only by the smaller proportion of particles with longer ranges or by the effects of gamma radiation if the dose is sufficiently increased. If the dose is too large then risks of focal necrosis causing in some cases minor thyroid crises or late fibrosis of stroma may have to be faced. Larger doses do produce an undue proportion of cases of late hypothyroidism.

A test dose of I^{131} of small amount is given and with Geiger-Müller counter mechanism the proportion of the dose in the thyroid at a given time is estimated. Clinical measurement of the thyroid gland is made in an attempt to estimate its volume and mass, but

such estimates do not have greater accuracy than $\pm \frac{1}{3}$ of the true volume even in the most experienced hands. Then it is possible to calculate how much I^{131} must be administered to give an uptake of the required number of μc/gm. of thyroid, and with further data this dose may be expressed in terms of energy absorbed per gramme of tissue. An uptake of 100 μc/gm. at 24 hours will yield approximately an interstitial dose of 10,000 r.e.p. per gramme (J. B. Hursch and J. W. Karr, 1951).

Overseas reports showed that with the administration of doses of larger order a larger proportion of the patients get a good immediate result with abatement of the toxicity, but a definite proportion show overdosage effect with subsequent myxoedema.

All past radiation experience shows that a required radiation effect on any parenchyma can be obtained more slowly though equally well with divided doses using repeated small dosage increments, but that large single doses damage stroma with resultant fibrosis, arteritis and late necrosis. The depressant effect on cell growth may be a cause of late malignancy. Radiotherapists are alive to these risks. No known cases have occurred, but it is felt that the course of safety lies in slowly produced results obtained if necessary with repeated small doses. There is no clinical or histological evidence to show that doses of the order of 10,000 r.e.p. will cause either focal necrosis or a possible late malignancy.

For the above reasons our Melbourne technique prescribed small, perhaps too small, initial doses and the production of a gradual effect. Histological structure and the physiological activity of cells cannot be predicted and dosage cannot yet be determined mathematically when it is impossible to measure the size of a thyroid gland *in situ* with accuracy of only $\pm$ 33 per cent.

While dosage has been calculated on percentage I^{131} uptake and estimated size of the gland, clinical judgment of dose is the final arbiter, taking into consideration the degree of toxicity, the size of the gland, the percentage uptake and the values of serum Protein Bound Iodine.

Prior medications may have significance if I^{131} tests or treatment are contemplated. Previous administration of Lugol's solution, or the thiourylene drugs prevent I^{131} uptake, and all iodine-containing medicine should be withdrawn for at least two weeks and thiouracil for a minimum of 48 hours. Withdrawal of thiouracil drugs in acutely toxic patients even for a short time may cause embarrassment. I^{131} produces its therapeutic result slowly and three months must elapse before its major effect is attained. The patient therefore must be put back on medical treatment after the administration of the I^{131} while its effect is awaited, and according to the progressive response so the treatment may be withdrawn.

Original Australian supplies of I^{131} came from U.S.A., but they now come from England. Supplies are still limited and costly, though they are supplied free through the Health Department. The original policy of the Royal Melbourne Hospital group was to restrict treatment with I^{131} to those patients with thyrotoxicosis who had failed with either prior medical or surgical treatment. Our particular indications for I^{131} therapy of thyrotoxicosis are therefore found in the following groups:—

1. Recurrent post-operative thyrotoxicosis, particularly if vocal cord paresis is present.
2. Uncontrolled thyrotoxicosis following administration of antithyroid drugs—some such patients have been unresponsive, some sensitive to the drugs.
3. Progressive exophthalmos associated with severe toxicity — such cases often being regarded by the physicians as being made worse by surgery.
4. Thyrocardiacs — that group of patients in whom obvious or masked toxicity may be associated with varying degrees of cardiac failure.
5. Those patients with psychic disturbances complicating thyrotoxicosis.
6. With supplies now becoming more plentiful there is appearing a group of patients, particularly primary thyrotoxics, who do not desire surgical treatment or whose physicians advise I^{131} therapy.

Dosage administration is simple and the oral route is now used with precautions to avoid contamination. The patient takes the iodine-containing fluid from a container with a straw, and the bottle is refilled with

dilutant fluid on three occasions so that all of the dose is taken. Hospitalization is unnecessary.

Risks of I^{131} therapy in the possible production of genetic effects or late malignancy have been fully considered by overseas workers, and such risks are regarded as negligible especially if small doses are administered.

The only real contra-indication is administration to mothers more than twelve weeks pregnant, for at this stage the foetal thyroid begins to concentrate iodine. It may safely be given in pregnancy up to the ten weeks' stage.

The dose levels needed in thyrotoxicosis do not produce any local reaction of thyroiditis or tracheitis.

Doses of moderate amount produce the result slowly and the full required effect may not be attained in the first dose. The alternatives are to administer larger doses or repeat further dosage of appropriate amount. Results of workers using doses sufficient to produce a high proportion of good results with a one-dose technique all show a significant proportion (6-10 per cent.) of ultimate hypothyroid cases. I feel that the only safe course lies in repeated administration of small dose increments—the aim should be to produce the desired result with two, possibly three doses. The results to date are shown in the following table:—

The above results indicate that patients have been underdosed rather than overdosed, and in the light of these figures the estimation of dosage has been reconsidered in an endeavour to produce consistent remission of the thyrotoxicosis in a shorter time — say in three to four months — using usually one or occasionally two doses.

The size of the gland is estimated clinically as very large, medium, or small. The clinical assessment of toxicity is graded as severe, moderate, or slight, while the measured uptake rate is recorded as high, moderate, or low.

From an arbitrary dosage level of 7 millicuries an amount of 2 millicuries is added for the large gland and 1 millicurie for the medium size, but 1 millicurie is subtracted for the small gland. The same amount is subtracted for cases with severe clinical toxicity because of the associated increase in radiosensitivity, and added if toxicity is low. Again, 1 millicurie is subtracted if the rate of uptake is high, or added in the opposite case.

So far no special dosage levels have been set for toxic nodular goitres, but experience may well show this to be possible.

THE USE OF I^{131} IN THE INVESTIGATION OF UPPER MEDIASTINAL MASSES

Among upper mediastinal tumours, substernal thyroid extensions are common. If

CASES OF THYROTOXICOSIS TREATED WITH I^{131} AT THE ROYAL MELBOURNE HOSPITAL

No. of Cases: Males 2 — Age Range: 47 - 53
Females 21 — 22 - 65

	No. of Cases	No. of Doses Administered					Response to Treatment			
		1	2	3	4	5	No Imp.	Imp.	Eu-thyr.	Hypo-thyr.
Recurrence after subtotal thyroidectomy	5	2		1	1	1		2	2	1
Severe progressive exophthalmos	5	1	2	2				1	4	
"Thyro-cardiac"	6	4	1		1		1 Died 3/12	2	3	
Anti-thyroid drugs contra-indicated	4	1	2	1				2	1	1
Elective I^{131} therapy	3	2	1						2	1

thyroid tissue content is present in the mass, then it should be detectable by its pick-up of I^{131}.

However, retrosternal masses may contain the whole of the functioning thyroid and then the whole of the thyroid radiation is found to come from the abnormal substernal site.

In other cases the substernal mass may be a relatively inactive colloid goitre mass with still functioning thyroid tissue present in the suprasternal notch area. Then considerable difficulty is found in distinguishing the radiations from the two contiguous sources, especially if the substernal mass is the weaker source. There is a fairly high level of background radiation arising in the upper chest, chiefly from the I^{131} content of the blood in the heart, great vessels and lungs.

So, while I^{131} in theory should readily give an answer to the question as to possible thyroid content of an upper mediastinal mass, the practical difficulties of interpretation of results are often very considerable. The test procedure is reasonably simple and is well worth while when definite negative or positive results mean so much, but equivocal results with no diagnostic help forthcoming must be expected occasionally. Techniques are adequate to make the test worth while in all cases where a mediastinal tumour may be of thyroid origin.

Results:

10 cases have been investigated at the Royal Melbourne Hospital.

6/10 showed uptake indicating thyroid tissue present; all were verified at operation.

2/10 of the masses showed no indication of uptake; at operation a neurofibroma or a teratoma was found.

1/10 patient a thyrotoxic with a mediastinal mass. Toxicity accounted for by thyroid activity—no pick-up in mass.

1/10 test equivocal and diagnosis not established to date.

I^{131} AND CARCINOMA OF THE THYROID

I^{131} may be used therapeutically if the tumour tissue is sufficiently differentiated to pick up and retain amounts of I^{131} which would yield an effective quantity of radiation.

Carcinoma first grows as an undifferentiated tissue which only later may differentiate, and evidence of active thyroid function is to be seen in some such specialized areas. But the anaplastic growth must always be a step ahead of the differentiated tissue which is capable of I^{131} pick-up, and so such therapy holds little possibility of ever being curative.

In general, the carcinomatous thyroid loses its physiological functions and so its capacity for I^{131} pick-up. Significant pick-up does occur in the highly differentiated follicular thyroid carcinomas, but these are a small minority of malignant thyroid tumours. The common papillary adenocarcinoma shows little pick-up and the anaplastic group behave similarly, but occasional tumours in these categories show some take-up which can be increased under circumstances of complete suppression or extirpation of all normal thyroid tissue.

In the presence of metastases of such tumours complete ablation of the thyroid is followed by increased functional activity of the neoplastic tissue, as indicated by absence of the hypothyroid state, increased iodine utilization by the tumour and some restoration of P.B.I. blood levels. Further, the functional level as indicated by I^{131} pick-up can be sometimes increased by the use of thyrotropic hormone or thiourylene drugs.

A patient with a carcinoma of the thyroid and metastases should have a tracer test to determine if any degree of functioning is present, but even if any uptake is found, it is minimal in the presence of active normal thyroid, even in a highly differentiated follicular carcinoma.

In the pre-operative preparation stage a dose of about 1 millicurie of I^{131} is administered before surgery of ablation of the thyroid and the excised tissue is used for autoradiographic studies. A section is placed on a photographic plate which, when developed, shows the sites of I^{131} pick-up by local film blackening. The section is then suitably stained *in situ* on the plate, when comparison of the pathological structure with the evidence of physiological activity as shown by I^{131} pick-up can be made.

In four of our cases investigated along these lines by Dr. John Forbes the tumour was found to be of anaplastic type without I^{131} pick-up, and so I^{131} therapy was not further contemplated.

In several of our cases carcinoma has recurred at the primary site or metastases have appeared many years subsequent to the removal of an apparently innocent tumour. When secondaries appear later, tracer tests are carried out and if there is any evidence of tumour pick-up, total surgical ablation of remaining thyroid is carried out immediately. Alternatively, destruction of such thyroid tissue can be attained by administration of therapeutic doses of I^{131}. Subsequently, further tracer tests of the primary and secondary areas are carried out and are followed by more therapy doses of I^{131}, which must be given at regular intervals of not more than four to eight weeks in amounts of 40-100 millicuries. One of our cases in which an interval of three months was allowed between treatment developed a thyroid crisis on administration of a large therapy dose, and so doses must be frequently repeated to stop such a possibility.

Large amounts of I^{131} are needed for such a treatment programme and difficulty has been encountered in obtaining adequate quantities. The I^{131} is flown out from Harwell and supplied free by the Department of Health.

Four of our cases have received treatment, but all partly on account of supply difficulties have been underdosed. In view of the costs involved, the Standing Committee on Radioisotopes of the National Health and Medical Research Council will only make I^{131} available for therapy of selected cases of thyroid carcinoma of well-differentiated follicular type. All cases of carcinoma of the thyroid should be investigated to see if they fall within this category.

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The physical work of the Panel has been under the supervision of Dr. C. E. Eddy, Director of the Commonwealth X-ray and Radium Laboratory. The physical investigation was initially carried out by Dr. T. H. Oddie and later by Mr. K. H. Clarke and Mr. R. L. Aujard. Necessary physical apparatus has been supplied by the Laboratory.

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Detailed clinical, biochemical and physical papers reporting the work of the Panel are in preparation.

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GLOMUS TUMOUR

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"It would puzzle a convocation of casuists
to resolve their degrees of consanguinity."

Cervantes: *Don Quixote*
Part I, Ch. VIII

DURING the last quarter of a century we have achieved an appreciation of the characteristics of small, painful subcutaneous nodules known as glomus tumours; from almost complete ignorance we have progressed to a considerable knowledge of their structure, nature and relations. This has been partly because numerous examples have been described from all parts of the world but also because, stimulated doubtless in part by the discovery of the tumours, there has been a clearer understanding of the normal structures with which these tumours are related.

Thus, many questions such as the significance of the general structure of these nodules, some of the distinctive forms which they may adopt and the nature of the predominating cells in them have been answered. There are many other problems. There seems still to be uncertainty as to whether they should be regarded as tumours (that is to say, neoplasms). Furthermore, there are nodules, structurally composed of coiled vessels with an abundant nerve supply, which resemble glomus tumours except that the components of the walls are more obviously muscle cells than the characteristic "glomus" cells. There is still lack of agreement regarding the degree of innervation of glomus tumours.

These are some of the problems that face us at the moment and to discuss these, as well as give a general review of the problem of the glomus tumour, is the purpose of this paper.

HISTORICAL NOTE

It is a common thing for us to imagine that before a condition, with which we are well acquainted, was accurately described and more or less precisely named it was virtually unknown. A brief consideration, however, of the remarkable observers of earlier centuries, who were the founders of much of our present day knowledge should suggest that this point of view is misleading. Indeed, Stout (1935) mentions that these painful nodules were known to Morgagni (who quoted a case of Valsalva's), Cheselden and Petit, amongst others in the eighteenth century. In the nineteenth century, the condition was known to Dupuytren and later to James Paget. Earlier, Wood (1812) had given clear clinical descriptions of his own cases as well as brief reviews of others which he had found in the literature. He employed the term "painful subcutaneous tubercle."

It is understandable that, with the introduction of histology, before normal structures had been adequately investigated, these nodules should have been grossly misrepresented. Chandelux (1882) described tumours which appear to have been of this type, as tubular epitheliomas, and regarded them as probably arising from sweat glands. Kolaczek (1877) and Kraske (1887) refer to them as angiosarcomata and this opinion, which extended in some quarters well into the present century, was responsible for their treatment on the idea of their being malignant tumours. Müller (1901) applied the term perithelioma.

The modern era of our knowledge begins with Barré (1920-1922) who described the clinical features of several cases of this kind. Pathological investigation of two of these was undertaken by Paul Masson who had already obtained and examined a similar case in 1916. A description of the histological features, which has been the basis of much of our present knowledge, was published in 1924. Other accounts appeared

in the French literature (Martin and Dechaume, 1925; Masson and Gery, 1927; Prolanoff, 1927). In the next year, an important paper (Greig, 1928), which was the first significant one in the English language, appeared and now reports of cases, recognized as being of this type, became frequent from various parts of the world; Stout (1935) quoted them in the chronological order of Switzerland, Rumania, Argentine, Germany, Belgium, Spain and U.S.A. Stout's paper and that of Bailey (1935) are excellent reviews of our knowledge of the condition up to that time.

Since then there have been several papers embodying groups of cases, such as those of Lendrum and Mackey (1939) and Lemmer (1948). In addition, there have been several accounts which give excellent reviews from the clinical and pathological point of view, such as those of Oughterson and Tennant (1939), Beaton and Davis (1941), Loeb (1941), and Murray and Stout (1942).

GENERAL FEATURES

As a steadily increasing number of examples has been collected, knowledge of these remarkable structures has similarly increased. In some regards the boundaries of the group have become more defined, though, at the same time, in others they have become less clearly circumscribed as different but apparently related structure have been discovered. The over-all result, however, has been a clearer definition of the average or typical examples. An examination of the problems raised by histologically different forms of tumour has led towards elucidation of the development, nature and potentialities of cells in vascular walls. This is one of the many examples in the last few years in which clinical and pathological study of condition has stimulated interest in information of the fundamental phenomena of a tissue or region.

Distribution

When the relation of the glomus tumours to glomus bodies was appreciated, it was not unnaturally concluded that the tumours would be found in the areas where glomus bodies were most numerous; thus, for a considerable time, the area of distribution was regarded as being somewhat limited — particularly to the peripheral portions of the limbs. Accumulation of experience, however, has shown that they are much more widely distributed.

The glomus bodies are closely related to the histologically similar structures: the carotid body, the aortic, jugular and vagal bodies and the coccygeal body. It is not proposed, however, to include tumours of any of these well-defined visceral bodies in the present group. Here we will consider:

(a) the best known and relatively common epidermal and subcutaneous tumours;

(b) those occurring in tissues of the locomotor system; and

(c) more deeply-seated examples.

(a) The small tumours are found immediately under the epidermis or in the subcutaneous tissue, frequently in the limbs, and they occur much more often in the upper than in the lower extremity (Bailey, 1935; Lemmer, 1948; Gold, 1950). Those occurring under the nails have attracted particular attention. Examples have been described from the face (Butz, 1940; Lemmer, 1948; Gold, 1950), the eyelid (Kirby, 1941), the neck (Kirchberg, 1936), and the axilla (Gumpel, 1939). Tumours have been described on various parts of the trunk and the buttock (Stout, 1935; Lendrum and Mackey, 1939; Gold, 1950) and examples have been recorded on the penis (Grauer and Burt, 1939). Thus, though there are some areas where these tumours are most likely to be found, there is no part of the subcutaneous tissue of the body where they may not be encountered.

(b) A tumour in the substance of the vastus internus was recorded by André Thomas (1933); this was associated with a typical skin tumour in the same patient. A further example in the triceps brachii was recorded by German (1945). Another example in the triceps surae is included in the present series (Case 28).

A tumour in the capsule of the knee joint was recorded by Hoffmann and Chormley (1941) and other similar examples have been referred to by Stout (1935). A characteristic tumour, lying within the substance of a terminal phalanx was described by Iglesias de la Torre, Gomez-Camejo and Palacios (1939); others occurring in bones

of the foot were recorded by Bergstrand (1937); possibly related to these is the example recorded and figured by Oughterson and Tennant (1939) in which a tumour was involving a phalanx apparently by simple pressure.

(c) A tumour of the mediastinum was described by Brindley (1949). This tumour was histologically typical in form but was rather larger than usual and was associated with four subcutaneous nodules of typical form. The intrathoracic tumour was apparently attached to the eighth intercostal nerve. This tumour is included in the present group and thus segregated from other tumours which occur in the mediastinum in the region of the aorta quite arbitrarily because these last occur at the site of well-recognized collections of normally occurring glomoid tissue. For the present this is probably desirable, since, in the present state of our knowledge, attempts to correlate tumours of structures which, though fundamentally similar, possess somewhat different functions, may give rise to confusion. Other visceral examples have been recorded in the literature, but there is some doubt as to whether they are indubitable examples of glomus tumours. It is desirable that only incontrovertible examples should be included especially at a stage when we are still groping towards a thorough understanding of these tumours.

An example of a glomus tumour in the submucous tissues of the mouth on the outer aspect of the alveolar margin of the maxilla is included in the series of cases recorded in this paper (Case 27). This example helps to emphasize the widespread distribution of these tumours throughout the body.

Sex incidence

At the stage when only a few cases had been recorded, the sex incidence appeared to be equal and, indeed, this has been stated recently (Beaton and Davis, 1941; Jackson and Balkin, 1946), but study of groups of cases indicate that there is a definite preponderance of males; thus the proportion of males to females has been given as 9:6 (Lemmer, 1948); 11:4 (Lendrum and Mackey, 1939); 17:7 (Gold, 1950). The 6 cases described and referred to by Blanchard were all males; and in the present series the proportion is 20:8. It has been noted, however, that most of the subungual cases occur in females (Stout, 1935; Murray and Stout, 1942).

Age

The age at which the condition is first seen ranges from the end of the first to the ninth decade with most of the cases appearing in the third, fourth and fifth decades. When allowance is made for the time which the condition has been present before treatment, the age of onset is obviously anything from one to thirty years earlier. However, perusal of a large series of case histories shows that the majority seem to develop, as far as can be determined, on the assumption that the time of recognition of the nodule is related to its onset, in the second to fourth decades; only a few begin in the first decade, including occasional examples in the first year of life (Adair, 1934; Grauer and Burt, 1939). This may possibly be correlated with the conclusion that glomus bodies only develop during the post-natal period (Popoff, 1934).

Familial incidence

Almost all of the cases have occurred sporadically, but an excellent example of familial occurrence is recorded by Kaufman and Clark (1941), 4 cases being observed in one family.

Multiple tumours

At first, only single examples were described and there was a period when cases of multiple nodules were regarded as an extraordinary phenomena. However, various reports have now accumulated (Touraine, Solente and Renault, 1936; Hval and Melsom, 1936). These multiple examples may be grouped together in one area, as, for example, four nodules in one finger tip (Plewes, 1911) or around a heel (Bergstrand, 1937). On the other hand, they may be scattered diffusely over the body (Slepyan, 1944). The tumours may be very numerous; thus, in Slepyan's case, there were 12 nodules but as many as 48 (Weidman and Wise, 1937) and even 90 (Evster and Montgomery, 1950) tumours have been encountered in one patient.

Duration

The length of time that the condition has been present when treatment is sought varies very greatly—from a few months up to forty years. In recent years, however, the

tim interval has been short. This is largely du with adequate modern treatment, to the severity of the symptoms; although an occ sional patient suffers for a considerable tim before relief is obtained. Many of the lon standing cases have not had severe syn ptoms or have been able, by protection of he area, to avoid severe pain. In view of he symptomless character of some of the tumours, the length of time that the condit n has been noticed to be present may not be a real indication of its true duration. Ho ever, this period must be considered in all cases when the age incidence of the con lition is being determined.

Relation to trauma

A history of injury was noted in some of the earlier series (Stout, 1935; Blanchard, 1941) and was stated to be present in as high as 50 per cent. of the cases (Theis, 1937; Grauer and Burt, 1939). In some cases the tumour has developed at the site of injury and there appears to be a definite relation; however, in many of the cases the injury is of an ill-defined type and not necessarily in the region of the nodule and, as frequently happens in other conditions, may have merely drawn attention to the tumour. In 24 cases described by Gold (1950), only 2 gave the history of injury; in the present series there was a somewhat vague history of injury in 5 (only convincing in one) of the 28 cases.

SYMPTOMS AND SIGNS

A characteristic of this condition is that the symptoms, when present, are often arresting in their intensity but signs are minimal or even absent. In some cases, in the absence of a nodule, the diagnosis may be very difficult and the condition may be regarded as functional.

Pain

This varies very much from case to case in its site, type and intensity. In some cases there may be no pain at all, whilst in others it may be so severe that the patient demands amputation of portion of the limb.

The site of the pain may correspond precisely with that of the tumour and, indeed, may draw attention to the small nodule. At other times the nodule may not be apparent and this particularly applies when the tumour is in the subungual region. Again, the pain may not correspond with the position of the tumour but be at some little distance from it.

Though often localized to a small zone, considerable areas may be involved. The pain may radiate up a limb towards the body and may involve part of the trunk. In the most extensive cases as much as half the body may be affected. Occasionally a limb other than that containing the tumour may be the site of the pain. Portions of a limb or the trunk affected do not correspond with areas of innervation of nerve trunks.

The type of pain varies greatly. As stated, it may be absent and this, at one time regarded as a rare phenomenon, is well demonstrated in those cases of multiple tumours in which only some show pain or tenderness. In one case with 48 tumours, none was painful (Weidman and Wise, 1937); of 12 tumours, one was painful (Slepyan, 1944); of 90 tumours, 2 were painful (Eyster and Montgomery, 1950) and in the present series, in one case which showed 26 tumours only one was painful. The minor degrees are in the form of localized discomfort, perhaps on pressure, mild tinglings or merely localized "sensitiveness" in the area. These minor symptoms are often present in the early stages of cases which later show more severe disturbances. The pain is often described as burning, stabbing or shooting in type and excruciating or agonizing in intensity. It is usually paroxysmal in character, the attacks once begun lasting for some time.

In some cases the attacks appear to be spontaneous but, in others, definite initiating factors may be observed. These range from light touch to pressure of various degrees but, particularly in the later stages, in general the initiating factor is a very mild one. There appear to be certain "trigger points," stimulation of which gives rise to the attack. Alterations in temperature may be responsible. In general, increased warmth is responsible (Bonnet, 1927; Greig, 1928; Masson, 1924; Raisman and Mayer, 1935; Theis, 1937) but, on the other hand, cold has been known to usher in the attack (André-Thomas, 1933; Ianichewski and Lebel, 1928).

Tumour

The nodule may be observed by the patient himself in the form of localized reddish, purplish or bluish swelling of the skin and this applies particularly when the pain is localized to the region of the nodule. Sometimes he remembers having observed a small nodule before the pain became prominent. The nodule may be well-defined and cause a projection in the skin or may be less clearly demarcated, depending on whether the nodule is immediately under the skin or in the subcutaneous tissues. In the absence of the characteristic pain it is unlikely that the diagnosis will be made before the nodule is removed and examined histologically.

Vascular changes

These are of two types: (a) in the nodule and (b) in surrounding tissues.

(a) The degree of vascularity of the glomus tumour itself varies somewhat and this is particularly true in those patients in whom there are attacks of pain. During these attacks there is engorgement and swelling of the tumour (Wood, 1812; Bailey, 1935; Beaton and Davis, 1941).

It has been considered that the swelling of the vessels of the glomus tumour exerts pressure on the nerves in it and thus is directly responsible for the pain. In support of this there is the observation of Mason and Weil (1934) that when the blood was squeezed out of the tumour by gentle pressure pain disappeared but re-appeared when the vessels filled again.

Tissues in the neighbourhood of the tumour or even the whole limb may have a temperature different from that of the opposite side; in some cases it is significantly warmer (Bailey, 1935; Stabins *et alii*, 1937) or colder than its fellow (Lendrum and Mackey, 1939). This increased or diminished warmth of the part may be more obvious during attacks. Removal of the nodule is followed by the return of the part, from this point of view, to normal.

Nervous changes

Sweating of mild or even gross degree may be seen in the region of the tumour or over a limb (Lee, 1938; Oughterson and Tennant, 1939). A Horner's syndrome was observed on the same side of the body as a subungual tumour and this recovered after removal of the tumour (Masson, 1924).

"Trophic" changes

Changes are observed in the skeletal muscles and tendons and in the skin on the side of the tumour and in its region. These are osteoporosis of the bones, atrophy of muscles and thinning and atrophy of the skin. Some degree of bony deformity may occur as the result of postural changes. These various disturbances may be due to disuse or to vascular changes which are clearly reflex in character.

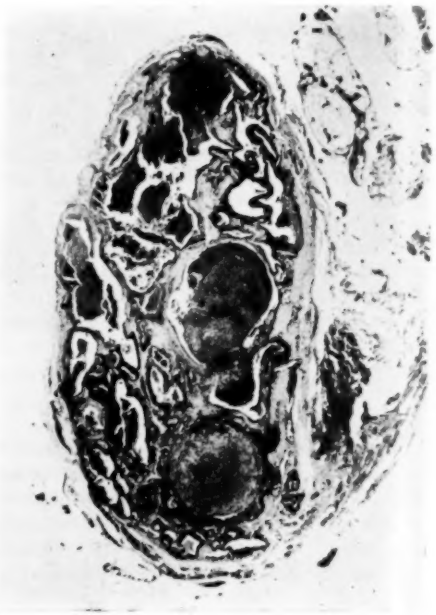

FIG. I. Photomicrograph of a section of glomus tumour (Case 1) showing the characteristic vascular structure. There is thickening of the walls due to the presence of the epithelioid cells. Some of the vessels are dilated. (x 1

PATHOLOGY

The morphological characters of the tumour are now well-understood and most of the difficulties arise from interpretation of well-defined appearances which themselves present but little problem.

Macroscopic appearances

As already mentioned, the tumours are found most commonly in the dermis and subcutaneous tissues (and particularly where glomus bodies are to be found) but they have also been observed in submucous tissue, in muscle, tendons and joint capsules and also in bone (Bergstrand, 1937; Iglesias de la Torre *et alii*, 1939). In this last position they may occur by erosion of the bone but may develop in the bone itself without any relation to extra-osseous structures. Tumours occurring more deeply appear to be associated frequently with nerves and these may be related fundamentally to the tumours which arise in those bodies associated with the vagus nerve and its branches.

Most of the tumours are small and they range from somewhat less than 5 mm. to 3 cm. or more in diameter. In shape they are ovoid or round, usually smooth and they may be lobulated.

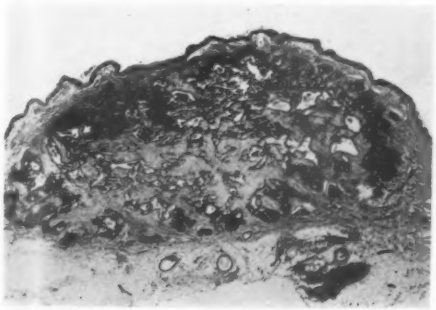

FIG. II. Photomicrograph of a superficially placed glomus tumour (Case 14). There are numerous vessels which are not grossly dilated and there are collections of glomus cells forming clearly-defined masses. The nodule has not a definite capsule but is sharply deliminated. (x 12)

On cross section they are homogeneous though somewhat fibrous in appearance and, in some of the more vascular forms, there are numerous dilated spaces filled with blood.

Usually there is a well-defined fibrous capsule (Fig. I), though occasionally the tissue merges with the surrounding connective tissue (Fig. II); this second type is probably the explanation for the cases in which recurrence has occurred after removal. It has been referred to as an infiltrating type of tumour by Stout (1935) and was so in his case, but in other examples it is probably a matter of a poor demarcation of the nodule from the surrounding tissues rather than a true active infiltration or invasion of them.

In some cases, although the affected area is well-defined, there is not a true capsule (Fig. III) and this is particularly apparent in cases such as that found in Case 6 in which numerous glomoid masses are scattered throughout the dermis and subcutaneous tissues over a considerable area (Fig. VI). It is obvious that in a case such as this incomplete removal of the affected zone would be followed by "recurrence" as it is in other types of malformations.

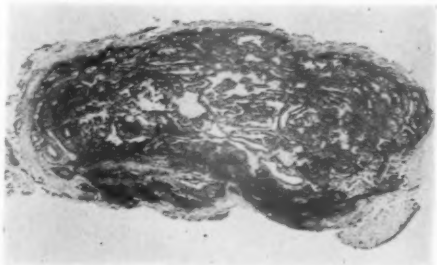

FIG. III. Photomicrograph of a section of a well-defined and encapsuled glomus tumour (Case 8). Here the vessels are not prominent and the tissue is obviously cellular. (x 10)

Histological appearances

The nodules are composed of numerous vessels which are the expression of a convoluted mass of blood vessels (Fig. IV). These are lined by a single layer of well-defined endothelium which may be flattened or swollen (almost cuboidal) in form. Surrounding this is a fibrous layer which, in some cases, is quite thick and very definite, but in other cases is very thin and delicate and requires special staining for its demonstration. Outside this there is a layer which varies considerably in thickness and is composed of the characteristic "glomus" or "epithelioid" cells (Fig. V). These cells have a well-defined outline and each is separated from its fellows by delicate collagen fibres. The cytoplasm is pale, and maybe vacuolated and the nucleus is round or ovoid, large, vesicular, and lies in the middle of the cell. Rarely are there any mitotic figures.

In the walls of some of the vessels there are some smooth muscle cells—some well-differentiated but others of an embryonal form. These cells may run either parallel or transversely to the long axis of the vessel. The cells may be intermingled with the epithelioid cells and usually they only occur to a predominant degree in the outer portions of the tumour. Near the periphery most of the cells may be of the smooth muscle type and, in and around the capsule, there are frequently vessels showing modified muscle cells only.

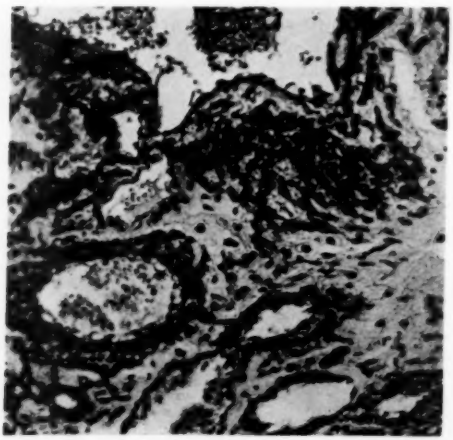

FIG. IV. Photomicrograph of portion of a glomus tumour (Case 3) showing vessels of different sizes with the characteristic "glomus" cells in the wall. (x 200)

The collagen fibres lying between the epithelioid cells are continuous, with more definite strands separating groups of vessels and communicating with the capsule. The stroma has a loose texture, sometimes referred to as oedematous, and mucoid change is sometimes observed in it (Fig. IX).

Usually there are easily recognizable bundles of myelinated nerve fibres near or in the capsule of the tumour. This may be correlated with the observation that some of the tumours have been in close relation to nerve trunks. In the tumour itself, there are numerous fine, non-myelinated nerve fibres, particularly beneath the capsule and in the stroma. These may be observed to pass amongst the glomus cells. This question of the demonstration of nerves has been one of the special points of disagreement between different writers. The technical difficulties in the demonstration of nerve fibres in many cases is well known: on the one hand, positive demonstration may prove difficult, and on the other, the capricious nature of some silver impregnation techniques results in the demonstration of fibrils which are not nervous in origin. However, with improvement in selective methods of staining and critical assessment of material and the results obtained, a clear demonstration of nerve fibres in these tumours has been made by many observers (Bailey, 1935; Stout, 1935; Blanchard, 1941). It has been suggested that the presence or otherwise of nerves may determine whether the tumours be painful or not. However, it has been demonstrated that nerves are present in both painful and non-painful types (Slepyan, 1944).

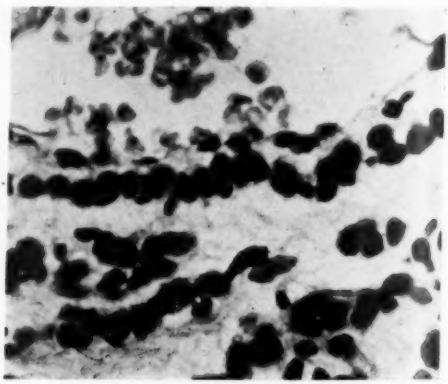

FIG. V. Photomicrograph of portion of a section of a glomus tumour (Case 8) showing a layer of glomus cells in the wall of the vessel. There is a layer of connective tissue between the endothelium and the cells. (x 700)

Types of tumours

The tumours may vary considerably in histological form depending on predominance of one or other component of the tissue. Several varieties can be described and various forms may be observed in different areas of one tumour. However, three main forms are usually described.

The normal type conforms with the appearances given above. The vessels are prominent but not dilated (Fig. IV). The zone of epithelioid cells is from two to five layers thick; there is a small amount of

con ective tissue and nerves are demonstrated in t e tumour itself, usually only by special stai s.

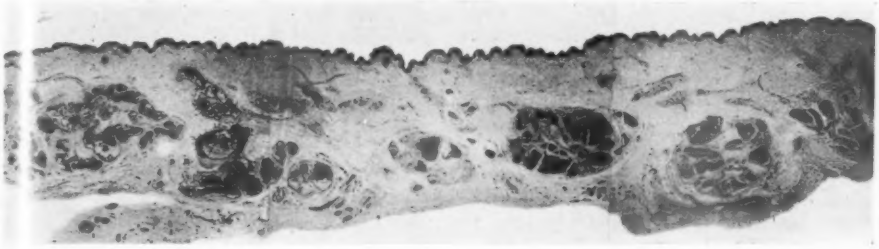

FIG. VI. Photomicrograph of portion of skin showing a series of "glomus tumours"; each of these is moderately well-delimited (Case 6). Most of them are of the vascular type and several have a well-defined capsule. (x 6)

A second type, often referred to as the vascular or "pauci-cellular" form, contains numerous widely dilated vessels filled with blood with relatively few cells in the wall and these about two layers thick (Figs. VII and VIII). This has been likened to a cavernous angioma and differs from it mainly in the presence of the glomus cells and there is rather more collagen in the wall of the vessels in these cases.

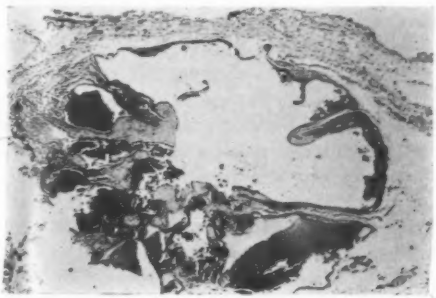

FIG. VII. Photomicrograph of a small glomus tumour (Case 12) of the vascular type. The vessels are greatly dilated, some containing blood-clot, but this has fallen out of others. (x 12)

In the cellular or "pauci-vascular" type (Fig. III and IX) the vessels have small lumens (recognizable because they contain erythrocytes) and around and between these there are numerous glomus cells. There is usually a relatively small amount of collagen between the cells. Indeed, the appearance is that of sheets of epithelium-like tissue which contain many small endothelium-lined spaces. Tumours of this kind are observed characteristically in the subungual region.

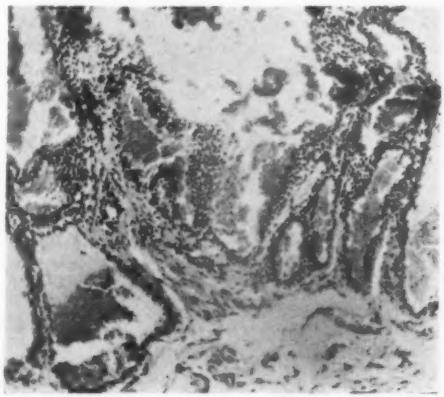

FIG. VIII. Photomicrograph of portion of a glomus tumour (Case 9) showing dilated vessels with "glomus" cells in the walls. (x 50)

In some cases there may be predominance of nervous, fibrous, or muscular tissue so that, in some examples, there are the characteristic appearances of a tumour of peripheral nerves, that is to say, a neurolemmona; in other cases there is a predominance of fibrous tissue so that the appearances are those of a vascular fibroma and in still others there is a predominance of smooth muscle cells. In all these examples the presence of a few "glomus" or "epithelioid" cells indicates the true nature of the condition. As mentioned previously, there may be oedema or mucoid change (Fig. IX) and this may be a predominating feature in the sections.

Nature of the "glomus" cells

A good deal has been written concerning the nature and origin of the "epithelioid" cells. They have been regarded as modified muscle cells, angioblasts or embryonic muscle cells, specialized neuro-muscular cells or as "pericytes." Most of these suggestions depend on the thoroughly unjustified view that any or each of these cells occupies a compartment separate and distinct from all the others. Such a view, not at all uncommon in current literature, is a remnant of the rigid and artificial notions of the last century and completely ignores all the evidence of a close and fluid or dynamic relation between similar cells. These various cells that have been mentioned are merely different stages of development of the same kind of cell or are comparable cells in different kinds of vessels, that is to say, capillaries and arterioles (Fig. X). The arguments completely ignore the demonstrable developmental changes that can occur during regeneration and healing in the adult and takes no account of the various stages of development that can be followed in different examples of glomus tumours or can be shown to occur in different parts of one tumour.

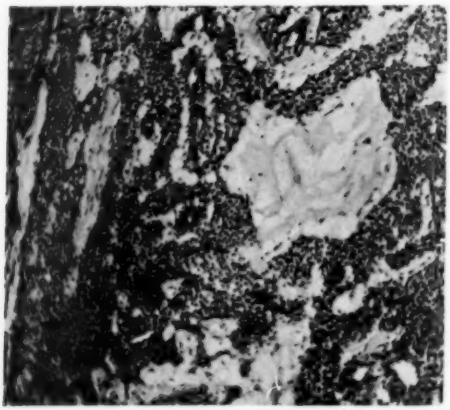

FIG. IX. Photomicrograph of portion of a subungual glomus tumour (Case 7) showing the typical appearance of the cellular variety. There is an area of mucoid change particularly apparent in one part of the connective tissue. (x 50)

These specialized "epithelioid" cell grow from cells in the walls of the vessels and, as shown by their reciprocal relation with muscle cells, have a close relation with these structures. There is some question regarding from which cells they arise and it is probable that they arise from more than one kind of cell; but the proposition that they constitute a separate and distinct type which is different in potentialities and origin from the well-recognized cells of capillaries, arterioles or venules is a misleading proposition and one which gives rise to many of our difficulties.

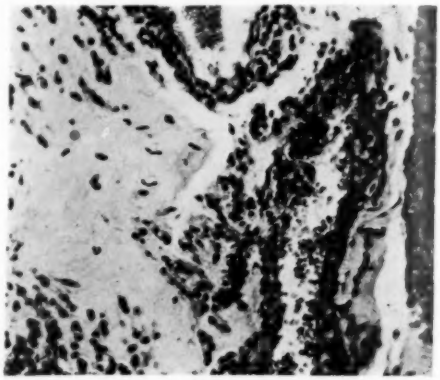

FIG. X. Photomicrograph of portion of a glomus tumour (Case 2) showing typical glomus cells in the walls of the vessels. Some cells are apparent also at a distance from the main vessel. (x 200)

It is important to realize that the development of any of these cells is dependent on the particular stimuli which are acting on the tissues and is not an inherent feature of the cells themselves. This means that, given the appropriate circumstances, the cells will arise in what were previously typical vessels, and, of course, this conforms with the knowledge that the glomus develops in post-natal life.

The nature and pathogenesis of the tumour

Although the condition is referred to as a glomus tumour it is important to remember continually that the term "tumour" is not always employed in the sense of a neoplasm. Ever since the early descriptions by Masson (1924) it has been recognized that this condition is well localized, usually encapsuled, slowly-growing and structurally is organoid—being an hypertrophied glomus

rather than a true tumour. The condition thus is of the nature of a malformation or hamartoma (Weidman and Wise, 1937) but in modern articles writers still refer to the nodules as if they were actually neoplasms and it is clear that some writers do not comprehend the fundamental propositions involved (Gold, 1950).

Artificial difficulties also arise in the question of the origin of the glomus tumours from glomus bodies. In some cases there may be a hyperplasia and hypertrophy of a glomus to form one of these tumours, but in view of the sporadic development of glomus bodies in post-natal life without any apparent rigidly determined preformation of such structures, an origin of a tumour from a preformed glomus does not need to be postulated. When this is appreciated, the development of glomus tumours in areas where glomus bodies are not known to occur normally (or occur in very small numbers) ceases to present a problem. Thus, just as a normal glomus body may develop from ordinary arterioles and capillaries, so the hypertrophied or hyperplastic structure also arises.

The problem of infiltration and recurrence of "tumours" after operation is important here because, at first sight, they suggest that some of the cases may indeed be true neoplasms. In most pathological conditions we find that a group does not have a sharp boundary but merges into other conditions; thus, in most cases, neoplastic examples of conditions which, in the majority of cases, are clearly not neoplastic do occur. This may well be so in the present cases. Stout (1935) described one example which he regards as being a true infiltrating tumour. Simple recurrence after operation does not constitute true infiltration because this may be observed in such conditions as cystic hygroma of the neck and axilla—conditions which are malformations. If a small peripheral extension of such conditions is left at operation (and this is very easy to do), then a "recurrence" will occur. It may be stated that infiltration, if it does occur in these conditions, is a rare phenomenon. Related to this is the question of metastatic development: metastasis is a very strong indication of the neoplastic nature of a tumour. However, no definite example of a metastasizing glomus tumour has yet been described.

Terminology

The earlier names, such as painful subcutaneous tubercle (Wood, 1812), angiosarcoma (Kraske, 1887) and perithelioma (Müller, 1901), have been referred to above. In recent times two kinds of names have been given. The first of these is exemplified by "tumour of neuro-myo-arterial glomus" (Masson, 1924). Such a term was applied to indicate the complicated nature of the condition and also to imply that it was not actually a neoplasm. The objection that has been raised is that such a term is too cumbersome for ordinary everyday use and in attempts to improve the position names such as glomangioma (Bailey, 1935; Lendrum and Mackey, 1939) and angiomyoneuroma (Oughterson and Tennant, 1949) have been employed. The great disadvantage of these simple, concise and apparently adequate terms is that they strongly suggest that the condition is really a neoplasm and this disadvantage outweighs the advantages of brevity and apparent simplicity. There does not seem to be any term better than that of simple "glomus tumour" which does not carry any special connotation and, in view of its wide-spread use over many years, should not now cause special difficulty.

DIAGNOSIS

There is no difficulty in diagnosis in cases in which there is pain. All that is necessary is that the possibility should be considered (Picard, 1931) in those conditions in which the pain is not localized and no obvious nodule is seen; if the possibility is not remembered, a diagnosis of neurosis is likely to be made. This has been noted several times in the literature, and occurred in four cases in the present series.

If pain is absent the diagnosis is not likely to be made accurately until histological examination of a nodule is made. It is to be remembered that tumours, other than a glomus such as angiomata and leiomyomata, may be associated with pain of localized distribution and sometimes severe type.

Histological diagnosis gives no difficulty since usually the typical "glomus" cells present a characteristic picture. It is necessary to remember, however, as mentioned above, that there are various forms of the tumour and different tissues may predominate so that in some cases there may be a close resemblance to an angioma, fibroma, fibromyoma or neurolemmoma. Since the glomus tumour merges into those conditions in which these other tissues may be exclusively present, the diagnosis of some intermediate forms may present some degree of difficulty, but, the presence of a number of glomus cells in the walls of the vessels will make the diagnosis definite.

TREATMENT

The only treatment of any avail is the ablation of the nodule. Attempts have been made to deal with the pain by sympathectomy but without success. X-ray treatment of the nodule has similarly been ineffective. On the other hand, complete removal of the nodule has been uniformly successful, and since the nodule is well-circumscribed this does not present difficulty. In the few cases where the nodule has not been well-circumscribed and a small portion has apparently been left behind, more complete removal has resulted in cure.

CASES

The general features of the present series of cases are embodied in Table 1.

The distribution conformed with that observed in other groups; thus there were 15 cases in the upper limb, 7 in the lower limb, 2 on the trunk, one on the neck and one on the face. One was found under the mucous membrane in the mouth and another in muscle. There were 5 subungual examples.

Taking the time at which the cases were observed, they ranged from the first to the eighth decade. The mean age was 41 years. An attempt to determine the age at which the condition began was abandoned because of the uncertainty of the histories (from the point of view of the presence of a nodule) in some cases.

The sex incidence showed a predominance of males over females in the proportion of 20:8.

More than half the tumours were quite small, being less than a half a centimetre in long diameter but some of them were large, measuring nearly 3 cm. in diameter.

Multiple tumours were found in 3 cases. In one, showing twenty-six examples, they were scattered over the limbs and trunk. In another, they were confined to the trunk, and in the third case they were confined to the area of an arm. One example was a diffuse lesion consisting of an aggregation, under an area of the skin, of numerous small glomus tumours.

There was no very definite relation to trauma in these cases. In one example, Case 9, there had been an injury to the region at which the glomus tumour developed and this was regarded as showing a definite relation. There were 4 other cases in which there was history of injury but in which the relation was regarded as indefinite. There was no evidence of injury at all in the remaining examples.

Regarding symptoms, there was severe pain in 11 cases, moderate pain in 8 cases, and only slight tenderness or sensitiveness in 6 cases. There was no pain at all in three of the examples. Of the cases showing multiple nodules in each case there was only one which was painful. In two patients the limb was warmer than the other side and this reverted to normal after removal of the tumour. In one case the limb was colder than its fellow and this recovered after treatment. In 4 cases, at a stage before the tumour was discovered and removed, the diagnosis of a neurosis was made owing to the presence of severe pain which was not explained on an organic basis.

Histologically, the tumours were of the types ordinarily described. There were 13 which fell into the "normal" category, there were 7 of the cellular or pauci-vascular type and 8 of the vascular type. Several of the tumours showed a considerable amount of other tissues such as smooth muscle in the walls of the vessels, particularly in the outer part of the tumours, extreme fibrosis, or a large amount of nervous tissue. In no case, however, did these warrant a diagnosis of any other kind of tumour to be made.

TABLE 1
GENERAL FEATURES OF CASES OF GLOMUS TUMOUR

Case	Age	Sex	Site	Size	Number	Duration	Relation to Trauma	Symptoms		Pathological Type	Remarks
								Pain	Colour		
1	38	F	Subungual finger	4 mm.	Single	4 yrs.	Nil	Radiation on pressure	Bluish	Vascular	
2	54	M	Arm	1.8 x 1 cm.	Single	10 yrs.	Nil	Severe on pressure	Purple	Typical but poorly developed	
3	34	F	Trunk and limbs	8 x 5 mm.	Multiple (26)		Nil	One—painful only	Some bluish	Vascular	
4	62	M	Finger	1 cm. x 6 mm.	Single	17 yrs.	Apparent after injury	Spontaneous but "shooting" on touch	Bluish	Normal	
5	59	M	Thigh	2 x 1.2 cm.	Single	6 yrs.	Nil	Extreme on pressure	Bluish	Normal	
6	20	F	Hand	2 x 1 cm.	Diffuse	Indefinite but long period	Nil	Nil	Bluish and pigmented	Vascular	Thought to be a mole
7	72	M	Arm	1.4 x 1.6 cm.	Single	21 yrs.	Nil	Extremely painful to touch	Bluish	Cellular	Arm cold
8	47	F	Subungual index finger	5 x 3 mm.	Single	4 yrs.	Nil	Severe with with radiation	Bluish	Normal	
9	32	M	Thumb	6 x 4 mm.	Single	10 yrs.	Blow to region	Moderate	Bluish	Vascular	
10	51	M	Calf	1.4 x 1 cm.	Single	28 yrs.	Nil	Slight soreness and tenderness	Bluish	Normal	
11	27	M	Subungual thumb	5 x 4 mm.	Single	14 yrs.	Nil	Severe radiating	Bluish	Cellular	Bone involvement
12	25	M	Trunk	1.6 x 1.2 cm.	Multiple (5)	8 yrs.	Nil	One—slight pain on pressure	Purple	Vascular	One only histologically examined
13	43	F	Finger	1.2 x 1.8 cm.	Single	16 yrs.	Nil	Sensitive radiation pressure	Reddish	Normal	Temperature of limb raised
14	28	F	Neck	8 x 5 mm.	Single	1½ yrs.	Nil	Sensitive on touch	Bluish	Cellular	Not sharply demarcated
15	10	M	Elbow	2 cm. x 1.2 mm.	Single	3 yrs.	Nil	Not painful	Bluish	Normal	
16	64	M	Leg	5 x 3 mm.	Single	25 yrs.	Injury drew attention	Severe radiating	Reddish	Cellular	Regarded as neurosis
17	36	M	Face	5 x 3 mm.	Single	4 yrs.	Nil	Sensitive only	Reddish	Normal	
18	44	F	Subungual toe	4 x 2 mm.	Single	16 yrs.	Nil	Extensive radiating	Bluish	Normal	
19	52	M	Knee	1 x 1.4 cm.	Single	26 yrs.	Nil	Nodule noted	Bluish	Vascular	
20	19	F	Arm	6 x 9 mm.	Multiple (3)	1 yr.	Nil	One—painful on touching	Bluish	Vascular	One only histologically examined
21	24	M	Ankle	1.2 x 1 cm.	Single	9 yrs.	Nil	Soreness and radiating pain	Reddish	Cellular	
22	68	M	Forearm	1 x 1.8 cm.	Single	14 yrs.	Site of pressure	Non-radiating pain	Slightly bluish	Normal	Arm warm
23	15	M	Subungual finger	6 x 4 mm.	Single	3 yrs.	Nil	Pain on pressure	Bluish	Cellular	
24	12	M	Thigh	2 x 2.6 cm.	Single	30 yrs.	Followed fall	Attacks on touching	Purplish	Vascular	
25	3	M	Finger	8 x 5 mm.	Single	5 yrs.	Nil	Extremely sensitive	Purple	Normal	Regarded as neurosis
26	3	M	Hand	10 x 4 mm.	Single	17 yrs.	Nil	Sensitive and painful	Bluish	Normal	Regarded as neurosis
27	2	M	Under gingival mucous membrane over upper jaw	6 mm.	Single	5 yrs.	Nil	Tenderness		Cellular	
28		M	Triceps-suræ	1.2 cm.	Single	2 yrs.	Nil	Extreme pain on pressure		Cellular	Regarded as neurosis

DISCUSSION

As has been observed, the general features of these tumours is now well-recognized and understood. The manner in which additions are continually being made to our knowledge, however, indicates that this is anything but complete. This is particularly well-shown in the distribution of the lesions. At first thought to occur only under the skin in the limbs, they had been shown to occur over the whole of the body and in such deeper structures as muscles, bones, and tendons, and even within the body itself. These last probably have a close relation to the tumours which occur at the site of the deeper glomal structures: the carotid body, the coccygeal body, the vagal and jugular bodies and the aortic bodies.

A study of the history of the glomus tumours shows that they are a good example of pathological conditions which have given considerable information regarding the normal structures with which they are related. From the pathological point of view, they indicate the possibility of much wider occurrence of glomus bodies, not only in the skin but in the deeper tissues of the body. From the physiological point of view, they give a number of clues to the possible mechanisms by which these bodies produce effects on surrounding structures; and the sensory and reflex vasomotor changes which can be demonstrated following mechanical stimulation of the glomus tumours provides information not easily obtained with the normal structures. Of course, with each additional piece of information further problems arise, but it is in this way that progress in any field of knowledge is advanced.

From this further information, it is apparent that glomus tumours and glomus bodies will be found to be much more extensive in distribution than is apparent even at the moment, and it is probable that even further deep structures of the same kind will be encountered.

An important point mentioned earlier is the relation of the tumours to previously existing glomus bodies. From what has just been said, it seems quite clear that the tumours arise by changes in vessels which are structurally normal in histological character. It seems probable that the factors which give rise to the normal body in the infant are similar to those which give rise to the tumour, and elucidation of these factors in either case will probably throw a clear light on the origin and nature of the other.

The nature of the process which gives rise to these nodules is now quite definite. Most of the differences in the statements made in the literature are due to a residual confusion from the poorly-defined views of the last century. Although it is well-known, and should be universally recognized, that a mass of tissue is not necessarily of neoplastic nature—and though there are a great many examples to exemplify this—some teachers still fail to make the distinction clear. A neoplasm is a proliferation of tissue which has become different from the original tissue in its capacity for growth and thus one of the most important features of a neoplasm is that it continues to grow. Masses of tissue which develop extremely slowly and appear to come to a final form must be placed in a separate category. Furthermore, neoplastic proliferations, although sometimes showing a considerable degree of organized development, do not give rise to the same degree of differentiation that is observed in the original tissue. When a mass of tissue is both morphologically and physiologically of the typical adult type, and this applies particularly when it is in the form of an organ rather than merely a simple tissue, it falls into the category of a hypertrophy or hyperplasia of the tissue and, when sufficiently gross, is to be regarded as a malformation. There are many examples of these in the body and the term "hamartoma" has been applied to them.

The slow development of a well-encapsuled structure, which has an appearance comparable with the original glomus, would indicate quite clearly the nature of the condition. Moreover, the examples in which there are multiple tumours emphasizes further the non-neoplastic nature of the condition and places it in the same group as multiple telangiectasis and other vascular conditions. The diffuse example in this

series (Case 6), in its morphological characters, its long history and absence of growth, is clearly a non-neoplastic condition and conforms with some of the naevi of various kinds seen in the skin and, at the same time, apart from the multiple glomal foci is a typical example of the condition.

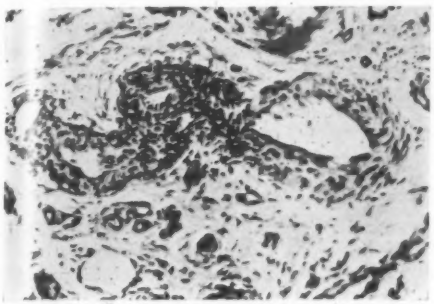

FIG. XI. Photomicrograph of a vessel at the periphery of a glomus tumour (Case 5). Part of the vessel is normal in character, having smooth muscle cells in the wall, but the remainder shows numerous glomus cells, occupying the "muscular" region of the wall. (x 150)

The mode of development is by an increase in the number of vessels in an area and change of the cells in the wall into the "epithelioid" or "glomus" type. From study of examples of the small specimens of glomus tumour it would seem that the process is not significantly different from the development of a glomus itself. Further, enlargement of the nodule occurs by change in the vessels at the periphery of it. This is indicated by the discovery of muscle cells in some of the vessels at the periphery and these merge into those which are typical in character without any "glomus" or "epithelioid" cells at all. In the vessels which contain both glomus cells and muscle cells these are not usually found intermingled although they may occur together in some areas (Figs. XI and XII). The relation of the cells indicates that they are similar in origin and that the type of cell occurring in any particular region depends on the direction of differentiation of the tissues in the vessel wall.

There is a considerable amount of apparent disagreement regarding the nature of the glomus cells. Most of this arises, as mentioned earlier, from a too rigid notion that any cell in the body must constitute a type *sui generis*. They should not be regarded as arising solely from muscle cells nor from "pericytes" nor is any improvement in our understanding gained by regarding them as being embryonal in character. They constitute a specific type of adult cell and constitute a particular differentiation; but the discovery of myo-fibrils in some of them shows that they have a relation to the muscle cells of the vessel walls. There is no definite evidence as to whether they arise from muscle cells or from precursors of muscle cells but it is likely that more than one kind of cell, in appropriate circumstances, may give rise to these. It is certainly probable that the cell from which they arise in the capillary is different from, though related to, that in the thicker vessels.

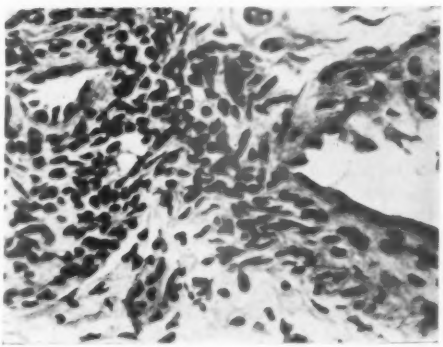

FIG. XII. Photomicrograph of portion of the section shown in Fig. XI showing the character of the cells in the wall. In the area where the glomus cells are apparent, some elongated muscle cells can also be seen. (x 350)

This brings us to the question of the relation of the tumours to other types of growth. As mentioned earlier, these various ones: the glomus tumour, various angiomata and vascular liomyomata, merge into each other and although the typical examples of each are quite distinct, they are related both in origin and nature.

The precise ontogenetic relations of these various cells is still not clearly understood but it would seem probable that elucidation of this is quite as likely to be made by study of glomus tumours and their relations as by

investigation of the normal structures. The continued extension of knowledge of the general characters of the tumours, even in recent years, is a good augury in this regard and shows that there is still much to be discovered about these structures.

SUMMARY

A review of glomus tumours is given, based on a study of the literature and investigation of 28 new cases.

Although distributed mainly in the dermis and subcutaneous tissues, they occur also in muscle, tendon and bone and in the deeper parts of the body, and though they are usually found singly they may also be multiple. They occur more commonly in males.

These tumours are not neoplasms but are malformations (hamartomata) of a characteristic structure, being composed of a network of vessels in all of which there are characteristic "epithelioid" or "glomus" cells. Smooth muscle, fibrous tissue and nervous tissue may occur in considerable amounts and occasionally may predominate. The tumours thus are seen to merge imperceptibly through various examples into vascular or muscle tumours of the skin and subcutaneous tissues. This may be correlated with the observation that some of these other types of tumour may show the characteristic clinical syndrome of severe pain of either local or radiating type. Although this observation is important as indicating the lack of sharp boundaries so characteristic of many pathological conditions and, in fact, of life, the typical tumour is a very characteristic structure.

ACKNOWLEDGEMENT

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TORULA (CRYPTOCOCCUS) INFECTION OF THE LUNG

By M. P. Susman

Sydney

THE organism *Torula histolytica* or *Cryptococcus histolyticus* is so widespread that man and animals are constantly exposed to infection. It seems to be essentially a pathogen and only rarely can it be dismissed as a contaminant. The central nervous system and the respiratory system are the commonest sites of infection, but any organ or tissue may be involved. There is no specific treatment, but spontaneous cure of pulmonary infection possibly occurs, and long remissions have been reported with meningeal torulosis. Most of the deaths occur from meningeal involvement. The combination of pulmonary and meningeal torulosis is so common that every patient with proved or suspected pulmonary infection should have his cerebro-spinal fluid examined, and conversely every patient with torula infection of the meninges should have radiograms taken of his lungs. It must be emphasized that these examinations should be made even if there are no pointing symptoms because there are now many records of symptomless meningeal and pulmonary torulosis. The absolute diagnosis depends on the finding of the organism either by direct examination or on culture. With torula meningitis, cells, usually lymphocytes, are found in the fluid, with a rise in total protein and a fall in sugar and chloride.

Two forms of lung infection have been described:—

1. A large collection of torula forms a solid slippery mass which casts a dense homogeneous radiological shadow; the rest of the lung fields are clear as a rule.
2. There may be small scattered collections of torula throughout one or both lungs, with surrounding peri-bronchial fibrosis and granulomatosis. Skiagrams show a series of irregular shadows and may even suggest miliary tuberculosis. Calcification may be obvious.

Torula causes a subacute or chronic response with little surrounding reaction, and caseation does not occur. Apart from one report of direct infection of three premature infants from cryptococci present in the maternal genital tract (Neuhauser and Tucker, 1948), there are apparently no proven cases of direct infection between man and man or man and animal. Often the lung appears to be the first organ affected and spread then occurs by the blood or lymphatic streams. Early removal of the lung focus may be curative, but it remains to be seen whether removal of the lung lesion in the presence of meningeal disease improves the prognosis. The difficulty of deciding this lies in the well-known tendency to spontaneous remissions and the possibility of natural cure.

Berk and Gerstl (1952) reported a case of a single torula mass in one pulmonary lobe and said that only five other cases of similar torular lesions had been recorded; but they omitted at least one earlier case, that of Starr and Geddes (1948), in which lobectomy was done because of an indeterminate opacity and the diagnosis was made on microscopical examination. I saw this patient in 1952 and he was then well and symptomless, with a clear skiagram. No torula were ever found in his cerebro-spinal fluid. Cruickshank and Harrison (1952), in reporting a case of pneumonectomy for a cryptococcal mass in the right lung, said that only six cases had so far been reported in Great Britain.

Baker (1952) reported three cases of pulmonary resection for torula (cryptococcus) infection; the immediate result was good in all three, with "follow up" of nine months, nine and a half months and four years respectively. He says: "Perhaps resection was prophylactic against the development of cryptococcosis of the central nervous system."

Three cases of torula infection were shown at the B.M.A. meeting at Sydney Hospital in

September, 1953, and Penington (1953) says that there have been six cases in Queensland this year.

In the Sydney Medical School there are specimens from two cases of torulosis of the lung and central nervous system.

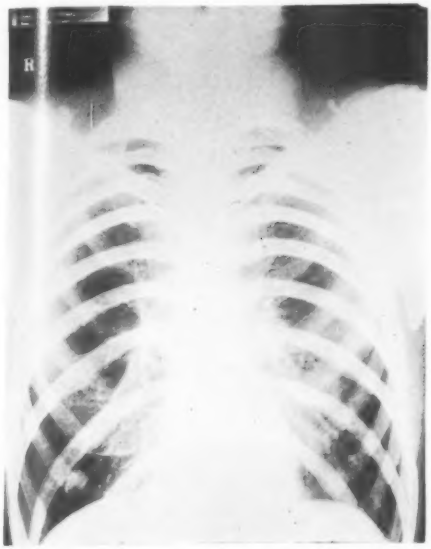

FIG. I. The opacity lies just above the right dome of the diaphragm, below the tip of the sixth rib. Tomography showed that it was in the posterior basal segment of the lower lobe. (Case 1)

I have three cases to report:—

Case 1

A man aged 38 was advised to have a thoracotomy because of a single round opacity at the base of his right lung. He had no symptoms or signs of disease and the radiogram was taken during a mass survey. The provisional diagnosis was tuberculosis. At operation on 27th October, 1952, Mr. Ian Monk found a "lump" in the right lower lobe which he removed by wedge resection. The specimen is circular and has diameter of 1.2 cms.; microscopical examination disclosed torula. The operation was performed thirteen months ago and the patient has been well and symptomless since. The cerebro-spinal fluid was normal when the patient was discharged.

Case 2

A man aged 60 was sent to hospital because a routine skiagram showed an irregular opacity at the base of the right upper lobe. He had no symptoms at this time, but soon afterwards he complained of headache and drowsiness and he died several weeks later in coma. Autopsy disclosed: (1) Torula infection of the membranes and of the brain; (2) A torula mass measuring 7 cms. by 4.5 cms. in the right lung, and scattered areas of broncho-pneumonia in both lungs.

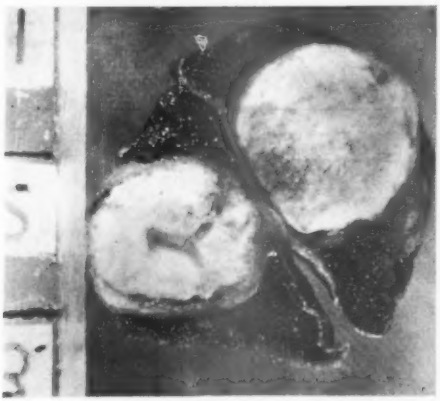

FIG. II. The torula lesion removed by wedge dissection. It measured 1.2 cms. in diameter. (Case 1)

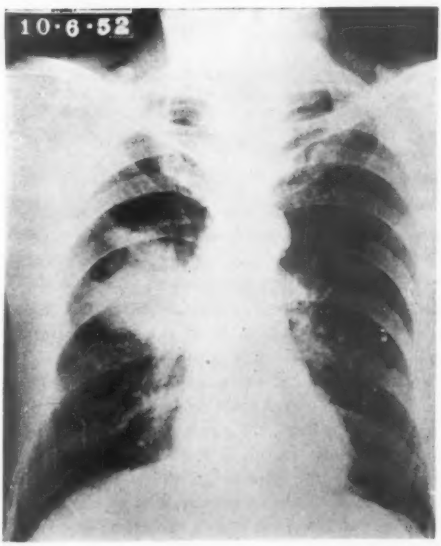

FIG. III. This opacity, in the base of the right upper lobe, was found in a mass X-ray survey. At this time, the patient was symptomless. (Case 2)

FIG. IV. This shows the torula mass in the right upper lobe. There were scattered patches of broncho-pneumonia in both lungs. (Case 2)

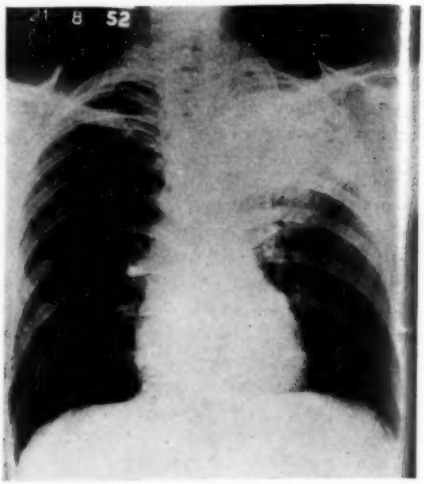

FIG. V. Dense opacity in left upper lobe. (Case 3)

FIG. VI. The upper lobe has been replaced by mass of torula. (Case 3)

Case 3

A man aged 43 said that he had had a cough for several years which had been worse in the last year; he had up to two ounces of sputum daily. Other symptoms were moderate dyspnoea, occasional night sweats, low fever and remittent headache. There were signs of consolidation of the left upper lobe and a skiagram showed a dense opacity. Every specimen of sputum examined and most specimens of the cerebro-spinal fluid contained torula. His condition remained good throughout. In spite of the meningeal involvement, left pneumonectomy was performed on 9th October, 1952, and he made a satisfactory recovery. Eleven months after operation he is well and at work. Some specimens of cerebro-spinal fluid since operation have contained the organism, others have been sterile but have had increased cellular content. He has little sputum and it is now free of torula.

SUMMARY

Three new cases of pulmonary torulosis are described. Two of them had proven torular meningitis. If there is no meningitis, pulmonary resection is almost certainly indicated if the lesion is localized. The question is posed whether it is justifiable to remove the pulmonary focus in the presence of meningitis.

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DELAYED TRAUMATIC INTRACEREBRAL HAEMORRHAGE
(TRAUMATISCHE SPÄTAPOPLEXIE)

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Alfred Hospital, Melbourne

THE term *traumatische Spätapoplexie* was first introduced by Otto Bollinger in 1891 to describe an intracerebral haemorrhage caused by, but occurring at some time after, a head injury. Since then there has been considerable discussion of the subject in its pathological, diagnostic, therapeutic and medico-legal implications, and sporadic case reports and reviews have appeared in the literature. Some authors deny the very existence of the condition, whilst others speculate upon the possibility that in any case of cerebral haemorrhage, a previous minor head injury may be of aetiological significance. Certain it is that well-authenticated cases are rarely encountered, and a large proportion of the few dozens of cases reported in the literature must be rejected as insufficiently proven.

This present contribution to the literature on the subject was inspired by the unusual occurrence of two cases within a few weeks at the Alfred Hospital. It is submitted that both cases fall well into the category of *Spätapoplexie*, but that the second case in particular is as well documented as any in the literature.

CASE REPORTS

Case 1

Mr. R.W., aged 53 years, was brought unconscious to the Alfred Hospital on the evening of 27th June, 1953. From his wife, the history was obtained that one week previously he had come home from work with a small dressing on the right side of his forehead. She asked its significance and was told that he had been struck on the head by a beam of wood which had bruised and dazed him, but he now felt quite well. During the week he had felt quite well and had behaved normally and gone to work as usual. On the day of admission he awoke with severe frontal and occipital headache which increased during the morning, and his behaviour was peculiar. During the afternoon he became increasingly drowsy and vomited. In the evening he was unrouseable, and admission to Hospital was advised.

He was admitted as a case of subdural haemorrhage under the care of Mr. H. A. Phillips. On examination in the ward he was found to have a healed abrasion at the right frontal hairline, but no evidence of fracture and a normal cranial percussion note. He was a well preserved man, with pulse rate of 70 per minute, blood pressure 165/95 mm. of mercury, and the peripheral vessels were not palpably thickened. He was stuporose, just able to be roused, and had equal reacting pupils and a minimal left spastic hemiplegia. There was considerable neck stiffness.

Lumbar puncture was performed, and some haemorrhage was encountered. Moderately and evenly bloodstained fluid was obtained at a pressure of 250 mm. of cerebrospinal fluid. It was thought that a subarachnoid haemorrhage was present apart from the trauma of puncture, but when the specimen was centrifuged, the supernatant fluid was clear.

A provisional diagnosis was made of spontaneous subarachnoid haemorrhage due to rupture of an intracranial aneurysm, though subdural haematoma was still considered a possible alternative diagnosis. He was kept under close observation.

The next day his general condition and state of consciousness was unchanged, but his left limbs moved well and there was some weakness and spasticity of the right lower limb. Plain skull radiography revealed no evidence of fracture, and the calcified pineal gland was in the midline. Cerebral angiography was performed by Dr. H. A. Luke by the percutaneous technique of carotid puncture, and the films demonstrated a shift of the anterior cerebral arteries to the right, good filling of the brain to the skull surface, and no vascular anomaly. Subdural haematoma seemed practically excluded, and a diagnosis of intracerebral and subarachnoid haemorrhage was established. On the following day a further series of angiograms was obtained. These films, antero-posterior, oblique and lateral studies of the arterial, capillary, and venous phases of the circulation from each internal carotid, confirmed the previous findings. Further, no aneurysm was revealed, and the cerebral vessels were regularly filled and even in contour, giving no suggestion of cerebral vascular disease. The space occupying lesion was poorly localized — the anterior cerebral artery shift to the right without pineal shift was evidence of an anteriorly situated left sided lesion, and the suprasellar portion of the left internal carotid artery was displaced slightly downward (see Figs. I and II).

The diagnosis of *Spätapoplexie* was now made, and it was decided that conservative treatment was advisable unless deterioration should occur.

On 1st July, the patient was less conscious and the left pupil was larger than the right, but reacted

briskly to light. Lumbar puncture was again carried out and bloodstained cerebrospinal fluid was obtained at low pressure—thought indicative of tenorial coning. The following day, there was further slight deterioration and surgical exploration was undertaken.

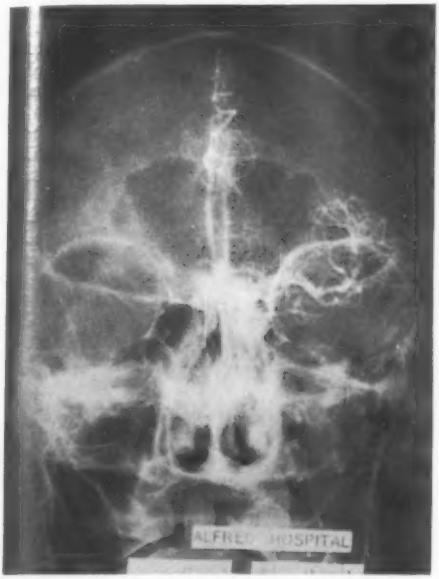

FIG. I. An antero-posterior projection of the left carotid arteriogram, showing displacement of the anterior cerebral vessels toward the right.

Under local anaesthesia, a burrhole was made in the region of the left frontal hairline, 4 cms. from the midline. Dura mater was opened, and the brain bulged strongly. A brain needle was passed medially, forward and downward through rather soft brain, and, at a depth of about 4 cms., dark blood clot and disrupted brain was obtained by aspiration, followed by a copious flow of bloodstained cerebrospinal fluid under considerable tension. The burrhole was then enlarged, cortex was incised, and a tunnel was made down to the clot with suckers and rongeurs. There was a large organizing firm clot medial to the anterior horn of the left lateral ventricle, and when this was removed there remained a cavity of about 80 ml. capacity involving both frontal lobes behind the anterior cerebral arteries. No aneurysm could be seen, and no particular bleeding point was found. The wound was closed with drainage, clear cerebrospinal fluid being obtained.

Post-operatively, his condition remained unaltered. His temperature ranged throughout between 102 and 105 F., without definite cause or other features of the neurogenic hyperthermia syndrome. On 5th July his respiration became rapid and bubbling, and numerous moist sounds were heard at the lung bases. As a good airway and dry lungs could not be maintained by postural drainage and pharyngeal toilet, tracheotomy was performed and much mucopus was aspirated. Thereafter there was little respiratory difficulty, but slow deterioration terminated in death on 8th July. Since death had followed injury, it was reported to the City Coroner, and no autopsy was performed.

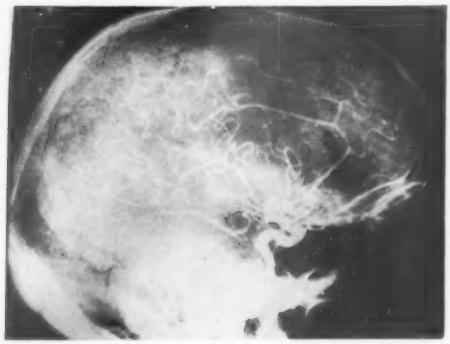

FIG. II. A lateral projection of the left carotid arteriogram showing some compression of the carotid syphon, but even contour of the vessels, with no suggestion of cerebral vascular disease.

Case 2

Mrs. M.Z., aged 39 years, was admitted to the Alfred Hospital under the care of Mr. H. A. Phillips on 25th June, 1953. She did not speak English, but it was gathered that she had been alighting from a bus when, laden with parcels, she had slipped and fallen on to the back of the head. She felt well except for a severe occipital headache. Her previous health had been excellent.

She was fully conscious on admission. A small laceration on the right occiput had been sutured in Casualty. The pupils were equal and reacted briskly to light, there was slight neck stiffness, and the right plantar response was equivocal. Her blood pressure was 120/85 mm. of mercury, and no other abnormality was found. X-ray examination of the skull (Fig. III) showed a vertical fine fissure fracture from the right occipital region crossing the transverse sinus into the posterior fossa. I was asked to see her on the third day because of persistent neck stiffness and a temperature of 100°F. Lumbar puncture revealed moderately bloodstained cerebrospinal fluid at a pressure of 140 mm. of cerebrospinal fluid, and cerebral laceration with traumatic subarachnoid haemorrhage was diagnosed. In view of the site of injury and the course of the fracture, close observation was maintained in case of posterior fossa complications. On 5th July she was discharged home, quite well except for slight occipital headache.

Two days later, she awoke feeling very well, but later complained of sudden severe frontal headache, vomited, and lost consciousness. Vomiting continued and she was quite unrouseable when re-admitted in the afternoon. There was some neck stiffness, the eyes were roving but not conjugate, the pupils were equal and reacted to light, and the right plantar reflex was extensor. The right limbs were rather flaccid or hypotonic. The pulse rate was 60 per minute, and the blood pressure 130/90 mm. of mercury.

FIG. III. An antero-posterior plain radiograph of the skull, showing a vertical right occipital fracture crossing the transverse sinus into the posterior fossa.

She was diagnosed as suffering from an intracranial haemorrhage, and posterior fossa extradural haematoma was considered likely, subdural hygroma being the other diagnosis entertained at this stage. Under local anaesthesia, surgical exploration was undertaken, and four occipital (a supra- and an infra-tentorial on each side), a left parietal, and bilateral temporal burrholes were made. No local lesion was encountered, but the brain was obviously under increased pressure. Post-operatively there was no change, and a close watch was kept during the night. The next morning, lumbar puncture revealed bloodstained cerebrospinal fluid.

Spätapoplexie was now suggested as the diagnosis (with the recent Case 1 in mind). Conservative management was decided upon as long as the patient's condition remained satisfactory.

Deterioration of consciousness occurred during the afternoon, and the right hemiplegia became more definite. Air ventriculography was now performed. Brain needles were inserted into each lateral ventricle through the upper occipital burrholes, and through the right needle clear cerebrospinal fluid was obtained under high pressure, whilst from the left needle ran almost pure dark blood. About 15 ml. of air was introduced into each ventricle by cautious fluid replacement, and X-ray films were exposed. The antero-posterior exposure (Fig. IV) showed good filling of the body and the frontal and temporal horns of the right ventricle, and of the body of the left ventricle. The ventricular bodies were displaced 2 cms. to the right. In the left frontal region was an irregular air shadow 5 cms. across and 3 cms. deep. The left lateral projection (Fig. V) showed the right (uppermost and therefore, air-filled) ventricle to be normal in outline. The right lateral projection (Fig. VI) showed the left lateral ventricle to be irregular in outline with gross distortion of the frontal pole. Neither lateral projection depicted the left frontal supernumerary air shadow seen in the antero-posterior film. A lateral exposure in the brow-up position was then made and showed (Fig. VII) that most of the air had escaped from the left ventricle into an irregular crescentic cavity in the frontal lobe.

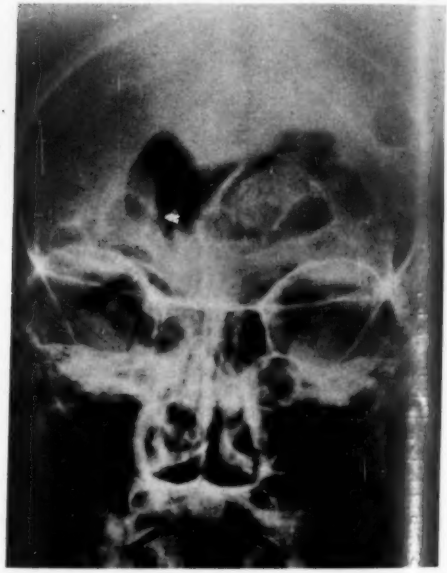

FIG. IV. An antero-posterior projection of the ventriculogram, showing marked displacement of the anterior horns of the lateral ventricles to the right, and an irregular large air-containing cavity in the left frontal lobe.

Thus was the diagnosis of a large space occupying haematoma in the left frontal lobe and communicating with the ventricle established. Operation was considered urgent.

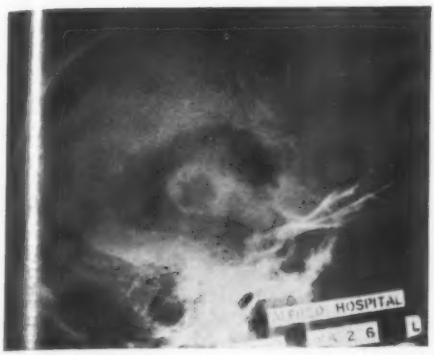

FIG. V. A left lateral projection of the ventriculogram, showing normal contour of the right lateral ventricle.

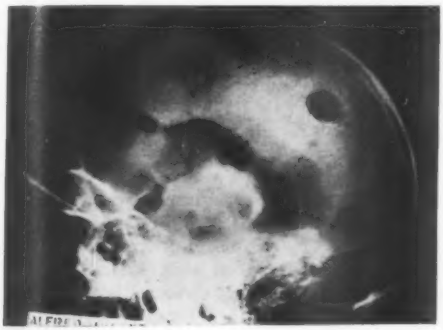

FIG. VI. A right lateral projection of the ventriculogram, showing the left lateral ventricle to be markedly deformed (anteriorly by pressure, and elsewhere presumably by contained clot).

A left frontal osteoplastic flap was cut with the Trumble craniotome, and turned down on temporalis. Through the dura could be seen the bruised and torn frontal lobe, and a dural flap was reflected. In the region of the Sylvian fissure was an area of old cortical bruising (as seen from the colour of altered blood). Extending upward and forward from the region of the sphenoidal ridge was a frontal lobe rupture about 5 cms. long through which protruded dark blood clot. The cortical margins were coagulated by diathermy current, and the clot was gently teased out. A cavity was now entered containing much dark blood and air, and when this had been evacuated the frontal horn of the ventricle was seen to have been opened, and eventually fairly clear cerebrospinal fluid was obtained. The only bleeding vessels encountered in the cavity were situated on its posterior wall in the region of the head of the caudate nucleus, and these were respectfully treated by packing them with a "gelfoam" slab, rather than by dissecting them out for diathermy coagulation in perilous territory. The raw cerebral surfaces were dressed with "gelfoam," the dura was sutured with subdural drainage, the bone flap was wired back, and the scalp was sutured with silk.

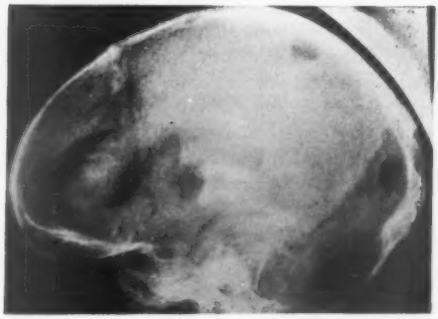

FIG. VII. A left lateral projection of the ventriculogram in the brow-up position, showing the anterior horns of the lateral ventricles, and the irregular crescentic frontal air shadow.

FIG. VIII. A diagrammatic representation of the relationship of the sphenoidal ridge, the Sylvian bruising (shaded area at tip of retractor) and the cortical rupture (at the site of the protruding clot), as seen at operation in Case 2.

Over the succeeding two days there was steady improvement until she was speaking to her relatives. Then there occurred a temporary relapse of drowsiness associated with pyrexia, neck stiffness and a cerebrospinal fluid leucocytosis. No organisms could be stained or cultured, but penicillin 1,000,000 units two-hourly and sulphadiazine one gram four-hourly

were exhibited as for meningitis. Thereafter there was uneventful recovery, and she was discharged from Hospital, seemingly normal, on 23rd July.

COMMENTARY

The first patient suffered an apparently very minor head injury but it resulted in death. The second patient suffered a rather more severe injury, but the mechanism of injury was trivial and common enough, and she was fortunate to recover from a perilous complication. In both cases there was apparently complete recovery from the effects of trauma before the onset of serious illness —a lucid interval of seven days in the first case, and twelve days in the second. Were it not for the fact that such an interval is well recognized to hold particular significance in cases of head injury, it is likely that the subsequent event might readily be considered to be unrelated to the original trauma. But a picture of space-occupying intracranial haemorrhage is readily conjured up by such a story, and extradural or subdural haematoma, in particular, is likely to be diagnosed.

The first patient was admitted with a diagnosis of subdural haemorrhage, which was reasonable enough. But the clear history of perfect normality followed by sudden severe frontal and occipital headache, vomiting, and increasing unconsciousness suggested rather the occurrence of a subarachnoid haemorrhage. Further, the findings of pupillary normality, neck stiffness, and minimal localizing signs supported this diagnosis, whilst the lumbar puncture finding of blood confirmed it. There was some difficulty in determining that subarachnoid haemorrhage had occurred, since the centrifuged specimen showed clear supernatant cerebrospinal fluid (it usually becomes xanthochromic in about two hours), but the whole clinical picture was strongly suggestive of ruptured aneurysm. Cerebral angiography, conducted as a thorough search for an aneurysm, failed to reveal such a lesion, but did show the presence of a space occupying lesion, and intracerebral haemorrhage could be assumed. Not all aneurysms are visualized by carotid angiography—if one is present in this case on the vertebral system it could not account for the site of haemorrhage, but a carotid system aneuurysm might not have filled because of the presence of clot. However, it is likely indeed that the process was simply intracerebral haemorrhage. It is regrettable that no autopsy could be conducted to confirm this opinion.

The second patient did not speak English, and when she was re-admitted the dramatic nature of the onset of headache, vomiting, and loss of consciousness was not appreciated. Had it been, the diagnostic possibilities would have resembled those in Case 1, aneurysm in particular being strongly suggested by such a story. However, in the presence of occipital injury, fracture crossing the transverse sinus into the posterior fossa, headache, lucid interval and loss of consciousness, and an upgoing plantar reflex, the diagnosis of posterior fossa extradural haematoma was made. These are the typical features of this condition, and the interval after injury was correct (usually seven to fourteen days). Nystagmus and other cerebellar signs are not commonly seen, the most usual being hypotonicity of the limbs (confused in this case, as often in the unconscious patient, with the flaccidity of hemiplegia). The diagnosis of posterior fossa extradural haematoma is to be made only if it is thought of in the appropriate case, and exploration is certainly required if doubt exists. Of possible supratentorial lesions, chronic subdural hygroma would be the most likely at this stage to cause severe headache and unconsciousness with minimal pressure and localizing signs. But the dramatic nature of the onset, when a clear history is obtained, bespeaks a sudden haemorrhage rather than the expansion of a surface collection. The mode of exploration on the first occasion seemed to have covered the likely possibilities, yet the lesion was missed. In the presence of good evidence of intracranial hypertension, immediate ventriculography might well have been undertaken, but the unpropitious hour and the apparently stationary state of the patient invited delay. The lumbar puncture the next morning was done with the realization that "coning" might be precipitated, and the early deterioration following it suggests that it was. The probable diagnosis of intracerebral haemorrhage was then reached, and localization and evacuation of the clot to relieve intracranial pressure became urgent.

Ventriculography was chosen in preference to carotid angiography since the latter shows properly only the anterior one-half to two-thirds of the brain, and this injury was

occipital. In fact, angiography would have localized the lesion adequately, but the finding of blood in the left ventricle and of an air filled cavity in the left frontal lobe was adequate reward for the decision. Curiously enough, on reflection, the diagnosis of intracerebral and subarachnoid rupture of an aneurysm was not even considered, mainly because the history was not accurately known.

At operation the whole picture fell into perspective. Whether the stationary head is struck on the occiput and so flexed on the cervical spine, or, whilst falling backward, the head is suddenly arrested, apart from local damage and complications one should always think of injury to the frontal region of the brain, particularly on the side opposite to the injury. The orbital surfaces of the frontal lobes are liable to laceration by rotation over the rough orbital plates, and the temporal pole to injury against the sharp sphenoidal ridge. In this instance, there was evidence of an old contusion (no old laceration to account for the initial subarachnoid haemorrhage was seen) in the Sylvian region, and the cerebral haemorrhage was immediately adjacent in the frontal lobe. It is to be noted that this haemorrhage did not extend to the medial or inferior aspects of the lobe, where an aneurysm might have been the cause, and that the frontal laceration seen at operation was patently fresh and due to rupture by the quite recent haemorrhage.

DISCUSSION

Traumatic intracerebral haemorrhages may be classified into three main types:—

1. Immediate.
2. Delayed—the true *Spätapoplexie*.
3. Late.

Immediate intracerebral haemorrhage may result from any head injury. In the case of depressed fractures it is not uncommon to find dural and cerebral laceration, with some surface blood and a sizable haematoma deep to the cortical laceration. On other occasions one finds an intracerebral haematoma deep to a laceration without depressed fracture, and recent experience suggests that when cerebral laceration is diagnosed in the presence of signs of increased intracranial pressure or of an extensive neurological deficit (suggesting deep extension of the lesion), perhaps exploration with a view to evacuation of such a haematoma should be considered. Occasionally a large intracerebral haematoma is found without cortical damage—the result of intracerebral shearing stresses. Of importance is the fact that immediate haemorrhage may present to the clinician as an acute, or as a chronic haematoma. In the latter case slow expansion of the lesion is presumed to occur until additional symptoms and signs lead to diagnosis, as in one of my cases (Jamieson, 1953). This sequence must be clearly differentiated from *Spätapoplexie*.

Late intracerebral haemorrhage occurs at an interval of some months or even many years following trauma, and is clearly attributable to that trauma since it occurs into a cyst resulting from colliquative necrosis of a contused area. This type again is distinct from that described by Bollinger as occurring usually some few days to three or four weeks after injury.

Spätapoplexie is a rare condition, if strict criteria be adopted for the inclusion of any case. Ritchie Russell (1932) reported one case, and referred to the condition as a "well recognized complication" of head injury. Dubois (1936) found 6 cases (excluding two late haemorrhages into cysts) in 1,700,000 consecutive hospital admissions. Symonds (1940) questioned the security of diagnosis in the cases of the previous two authors, reported a case which he considered doubtful, and described the condition as rarely encountered. The time of onset after injury of alleged cases varies from twenty-four hours to some months, but Bollinger's time interval is more usual, as in the cases described above.

In his original paper, based on 5 autopsies, Bollinger (1891) considered that injury produced an area of softening in which the wall of an artery became involved with subsequent rupture and haemorrhage. Langerhans (1903) was of the opinion that arterial disease always preceded the injury, which was but fortuitously related to the haemorrhage. A modification of Bollinger's view was introduced by von Holder (1904) who regarded the condition as a delayed haemorrhage into a small primary haemorrhagic focus produced by the injury. In both of the present cases the haemorrhage occurred

within the local field of a known brain injury, so that Bollinger's concept could well apply.

The manner of differential diagnosis from other post-traumatic space-occupying haemorrhages has already been considered. The sudden onset of headache, vomiting and unconsciousness at an interval after injury is unlikely to be due to extradural or subdural haemorrhage, whose clinical course is steadily, though sometimes rapidly, progressive. The importance of an accurate history, and the value of special investigations in difficult cases is also well illustrated. Two chief problems of diagnosis remain: the exclusion of ruptured aneurysm, and differentiation from the ordinary cerebral haemorrhage of cerebral vascular disease. Symonds (1940) particularly discussses the diagnostic difficulty of separating cases of cerebral aneurysm, stressing the similarity of clinical picture in the usual case and the fact that even angiography is not infallible in depicting aneurysms. In the first of the present cases, exhaustive bilateral carotid angiographic study on two occasions failed to reveal any aneurysm in the appropriate area, and nothing resembling an aneurysm was seen at operation when the whole haematoma was evacuated. Post-mortem examination would have rendered this search conclusive, but unfortunately was not permissible. The second case definitely was not due to ruptured aneurysm. The haemorrhage as seen at operation was well removed from any vessel prone to bear aneurysms, no aneurysm was encountered, and the source of haemorrhage was identified on the posterior wall of the cavity, deep in the hemisphere.

Some observations may be made regarding the possibility that these were cases of ordinary cerebral haemorrhage. The man was 53 years of age and had a blood pressure of 165/95 mm. of mercury, both of which facts suggest the possibility of cerebral vascular disease. But the peripheral and retinal vessels were normal on examination, and cerebral angiography revealed no vascular lesion. In the case of the woman, both her age, 39 years, and her blood pressure, 120/85 mm. of mercury, are against the diagnosis. Jewesbury (1947) discusses cerebral haemorrhage from the viewpoint that three-quarters of all cases involve the internal capsule, all other sites being atypical, so that special aetiological factors should be sought. In these cases, the coincidence of haemorrhage into an atypical area unrelated to a preceding trauma to it would be remarkable. The importance of making a diagnosis of *Spätapoplexie* is not purely academic, for it has therapeutic and medico-legal significance.

In treating a case of *Spätapoplexie*, one should keep two salient facts in mind: first, that many cases of atypical intracerebral haemorrhage recover without surgical intervention, which should only be invoked if deterioration of the patient's condition renders spontaneous cure doubtful; and secondly, that because of the atypical site of the haemorrhage, often well away from vital areas, the chance of successful surgery is greater than in ordinary cerebral haemorrhage. Harvey Cushing (1903) wrote of intracerebral haemorrhage in general: ". . . I believe that only in exceptional cases will surgical measures hold out any prospect of success . . . I do not see any reason why we should exclude these cases from the possibilities of surgical relief simply because the haemorrhage lies beneath the cortex, any more than that intracranial haemorrhage in other situations should be allowed to run its course." Jewesbury quotes a number of reported cases of successful surgery, to which this present one may be added.

The medico-legal situation is difficult indeed. It would be a brave, if foolish, man who would deny the possibility, in any case of cerebral haemorrhage, that preceding trauma may have been a factor. But when probability is to be decided, certain criteria may be suggested as a guide. The apparent severity of the trauma in question will often be of little assistance — in many of the reported cases, including those of Bollinger, it has been slight. The site of the haemorrhage certainly should coincide with the likely site of cerebral damage as suggested by the mechanism of the head injury. In particular, Courville and Blomquist (1940) have shown that the internal capsule is seldom damaged in closed head injuries, so that the ordinary capsular haemorrhage is unlikely to be precipitated by trauma. The time relationships of trauma to haemorrhage should be compatible with the understood pathology of the

co dition. For the diagnosis of *Spätapoplexie* on must ascertain the absence of ruptured an urysm or cerebral vascular disease, but ne her of these conditions excludes the pr bability that trauma may precipitate ha morrhage, indeed they increase the likeliho d though the importance of the trauma ov r the whole aetiological picture is dir inished.

CONCLUSIONS

1. *Traumatische Spätapoplexie* is a rare but definite clinical entity.
2. The pathogenesis suggested by Bollinger—that cerebral injury results in softening which involves a vessel wall —well fits the observable facts.
3. The mode of presentation imitates that of ruptured cerebral aneurysm, which condition and space-occupying surface haemorrhages require differentiation.
4. An accurate history of the illness is indispensable to diagnosis, and the early use of special radiological investigation is rewarding in the difficult case.
5. Surgical treatment of intracerebral haemorrhage in atypical situations should always be considered, and may be outstandingly successful.
6. Rigorous criteria should be adopted for the diagnosis of *Spätapoplexie*, and medico-legal opinion as to the probability that trauma has precipitated haemorrhage, should be cautious.
7. Apparently minor head injuries are not always trivial.

SUMMARY

1. Two cases of *Spätapoplexie* occurring within a few weeks at the Alfred Hospital are reported. One of them, in particular, is considered to be as well documented as any in the literature.
2. The methods of diagnosis from other complications of trauma, and from other "spontaneous" intracerebral haemorrhages are considered.
3. The various types of traumatic intracerebral haemorrhage are briefly discussed.
4. The pathogenesis of delayed traumatic intracerebral haemorrhage is thought to be that suggested by Bollinger in his original description.
5. The criteria for diagnosis and for medico-legal opinion are presented.

ACKNOWLEDGEMENTS

I am indebted to Mr. H. A. Phillips for the opportunity to treat these patients, and for his permission to report them. Mr. H. C. Trumble and Dr. J. A. Game saw the first patient and advised throughout his management. Dr. H. A. Luke performed the angiography in the first case, and the photographic reprints are the work of Mr. T. O'Connor of the Alfred Hospital.

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THE HEPATIC DUCTS. A SURGICAL APPROACH FOR RESECTION OF TUMOUR

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Introduction

RESECTION of carcinoma of the common hepatic duct or the lower reaches of the right and left hepatic ducts presents a difficult problem. Patients with neoplasm of the bile duct may come to operation without much delay owing to the early onset of jaundice, and if the growth can be excised, the prognosis is moderately good.

In 1952 there came under our care two cases of carcinoma of the junctional region of the hepatic ducts; in both the carcinoma was probably arising from the right hepatic duct. Using the approach to the porta hepatis about to be described, both these tumours were completely removed. In the older patient, however, liver failure and death resulted, but the younger man is still alive and well eight months later (Fig. VI). This type of case will not be encountered frequently, but it is wise for the surgeon to have a plan of attack should this condition be discovered at exploratory operation on a patient suffering from painless jaundice, and in whom neither the gall bladder nor the common bile duct are distended. This approach is therefore described in detail in the hope that it may be of value.

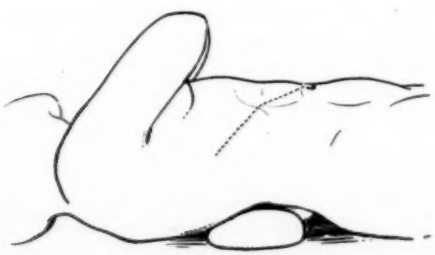

FIG. I. The line of incision and the position of the patient on the operating table.

FIG. II. The pleura and peritoneum are opened and the costal margin is divided. The diaphragm is divided towards the inferior vena cava opening.

Principles of the Operation

First stage: Decompression

These patients have considerable enlargement of the liver resulting from biliary obstruction and they are rendered ill from the liver failure which ensues. As a result it is our firm belief that preliminary decompression is of great value. This can be achieved by introducing a drain tube up the common bile duct past the tumour to drain the dilated duct system above it. This had been done by us as a palliative measure in two cases treated before the radical operation of excision was contemplated. With regard to the two cases about to be described, this measure was successful in one, but in the other a suitable channel could not be forced so the right hepatic duct was exposed in the porta hepatis above the obstruction, and a drain tube inserted at this level. It was found that exposure of the hepatic ducts on this occasion was facilitated by dividing Glisson's

capsule around the porta hepatis and dissecting upwards in a plane between the capsule and the liver. The level of the obstruction was gradually delivered from the porta hepatis and the normal ducts defined above this level. In both patients, three weeks after this decompression operation, the liver was found to be decreased in size and they were in better physical condition for a radical operation.

FIG. III. After division of the ligamentum teres and coronary ligament, the liver is rotated up into the chest cavity.

Second stage: Excision

The second stage of the operation consisted of a right thoraco-abdominal approach through the eighth interspace (Fig. I) dividing the diaphragm down towards the hiatus of the inferior vena cava (Fig. II). The liver was mobilized by dividing both the ligamentum teres and the coronary ligament so that it was attached only by the gastro-hepatic omentum at the porta hepatis and by the hepatic veins. The liver could then be rotated upwards partially through the slit diaphragm into the thorax so that the porta hepatis was facing upwards towards the operator (Fig. III). This enabled the duct system to be dissected free of the hepatic arteries and the portal veins up into the porta hepatis so that about two centimeters of right and left hepatic ducts could be mobilized (Fig. IV). The tumour, together with the gall-bladder and the supra-duodenal portion of the common bile duct could then be removed. The right and left hepatic ducts were anchored together by means of a single silk suture and the resulting figure of eight opening of the ducts were anastomosed by a single layer of interrupted silk sutures to a defunctioned loop of jejunum, using the "Roux-en-Y" method of anastomosis (Fig. V).

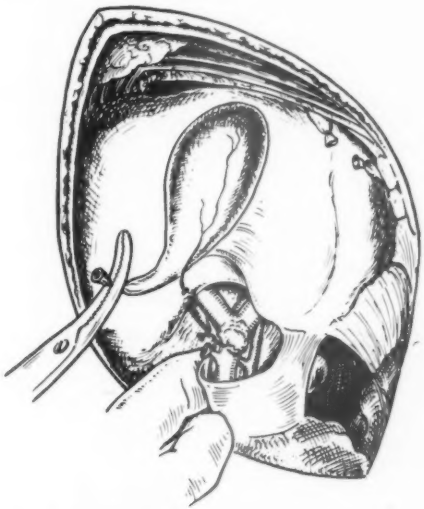

FIG. IV. The lesser omentum is opened and the bile ducts dissected out well up into the porta hepatis.

CASE REPORTS

Case 1

Mr. D.B., aged 35, was admitted to the Royal Melbourne Hospital on 21st Oct., 1952, with the history that six months previously he began to suffer fatigue, anorexia and abdominal discomfort. As a result of these symptoms he had to cease work. Ten days after the onset he observed that his urine was darker than normal and that his faeces were clay coloured. He consulted his doctor, who advised an operation. Three weeks later a laparotomy by another surgeon revealed what appeared to be "a gland obstructing the bile duct". A biopsy of the "gland" showed adenocarcinoma. The patient remained jaundiced, pruritus was severe and he lost much weight.

Physical examination revealed intense jaundice and gross enlargement of the liver. The enlargement appeared to be mostly confined to the right

lobe, the liver edge being palpable in the right iliac fossa. X-ray of the liver area disclosed no opaque calculus. The liver shadow was considerably enlarged. Alkaline phosphatase; 40 King and Armstrong units; cephalin flocculation, negative; prothrombin 100 per cent. of normal.

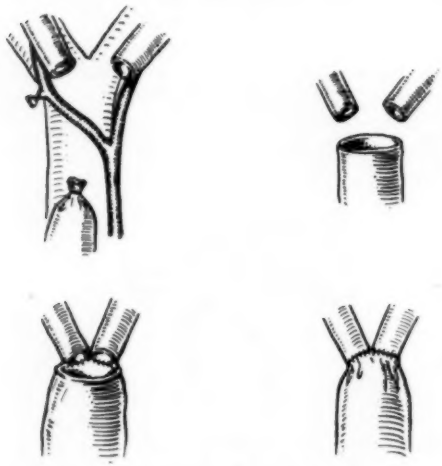

FIG. V. The tumour, lower reaches of right and left hepatic ducts, common bile duct, gall-bladder and cystic lymph gland are removed and the anastomosis completed.

Diagnosis and management. At this stage it appeared that the jaundice was obstructive in nature and that the most likely diagnosis was carcinoma of the hepatic biliary ducts—the evidence pointed to the right hepatic duct as being the site of the neoplasm. His physician, Dr. W. E. King, urged a further laparotomy with a view to confirming the diagnosis and assessing the possibility of palliative or curative surgery. Before operation the patient was given a full range of vitamin therapy and intravenous fluids.

Operation for drainage (30th Oct.). A right upper subcostal incision was made. The right lobe of the liver was grossly enlarged and had the macroscopic features of a biliary cirrhosis. The gall-bladder was not distended. A tumour was palpable in the porta hepatis. The common bile duct was opened and from it exuded a little bile-stained dark thick material. Sounds were passed upwards along the common bile duct and there was an obstruction to their passage into the right hepatic duct. This duct was exposed in the porta hepatis by opening Glisson's capsule and approaching the porta extraperitoneally. The right hepatic duct was opened and a considerable amount of "white bile" escaped. A specimen of the tumour was excised for biopsy and then a catheter was sewn into the right hepatic duct at the point at which it had been opened. A rubber drain tube was placed in Morison's pouch and the abdominal wall closed.

The biopsy report on the specimen excised during the operation was as follows—"A compact group of relatively well differentiated folded glands in fibrous tissue. The cells are very well differentiated in some parts, in a few places they are slightly irregular, nuclei being larger and more rounded and dark in colour. In most places the appearance is that of a papilloma, but in a few areas irregularity of cells suggests malignancy."

Post-operative period. Blood transfusions were necessary to control some peripheral circulatory impairment and there was some post-operative fever which was attributed to cholangitis. On the whole, however, the patient's condition remained most satisfactory. There was considerable drainage of bile from the catheter and with this there occurred marked lessening of the degree of jaundice and considerable diminution in the size of the liver.

Further investigations on 24th Nov. were: alkaline phosphatase, 20 units; cephalin flocculation, negative.

In view of the considerable improvement in the patient's general condition and liver function tests, together with the decrease in jaundice, it was decided to perform radical extirpation of the growth.

Operation for excision. On 8th Dec. excision of carcinoma of the hepatic ducts and choledochojejunostomy were performed.

A right thoraco-abdominal incision was made, the thoracic part of the incision running along the line of the anterior part of the eight left intercostal space. The abdominal and thoracic cavities were entered and the diaphragm incised. The ligamentum teres and coronary ligaments were divided and ligated. The fistula leading to the right hepatic duct was dissected and it was possible to identify the right border of the lesser omentum. The right lobe of the liver was then displaced upwards into the right pleural cavity and the porta hepatis explored. As the neoplastic mass was still circumscribed it was decided to resect it. The structures in the right border of the lesser omentum were identified and then the upper part of the common bile duct, the gall-bladder, the common hepatic duct and a portion of the lower part of the right hepatic duct were resected. The cut lower end of the common bile duct was ligated. All the malignant tissue present appeared to have been removed, leaving the left hepatic and most of the right hepatic duct *in situ*. A Roux-en-Y choledocho-jejunostomy was then performed. A drain tube was inserted to Morison's pouch and the wound closed. The tissue resected was reported upon by the pathologist as follows: "There is a papillary tumour on the surface of the hepatic duct; no invasion of the fibrous wall is present, except perhaps for one or two well-differentiated tubules below the general level. Considerable inflammation is present."

Conclusion. Papillary adenoma of hepatic duct, probably well differentiated carcinoma.

Following operation there was temporary peripheral circulatory failure, but the patient rapidly responded to resuscitative therapy. X-ray examination of the chest on the third post-operative day

reve led increased peri-bronchial markings at the righ base, but there was no demonstrable effusion or pne mothorax. On the fifth post-operative day he was able to sit out of bed. Investigations on the fou enth post-operative day were: alkaline phospha se, 18 units; cephalin flocculation, negative.

O the twenty-second day after operation he was disc arged home following a total period of seventy day in hospital. Following discharge the patient has remained very well. On 22nd Feb., 1953, the seru n bilirubin level was 2 units and when the pati nt was last seen on 10th June (eight months afte operation) he was feeling very well; he had gain d three stone in weight, there was no evidence of jaundice and he had returned to work as a carter (see Fig. VI).

FIG. VI. Photograph of Case 1 taken on 27th May, 1953, showing the extent of the incision and the obvious well-being of the patient.

Case 2

Mr. H. McG., aged 74, was admitted to the Royal Melbourne Hospital on 13th Dec., 1952, complaining of anorexia and jaundice. He had been quite well until three weeks previously, when he had noticed anorexia, nausea and flatulence. He had also noticed that his urine was dark and his motions were pale. Two weeks previously he had noticed jaundice which was accompanied by severe pruritis. He had had no pain, had not been in contact with any jaundiced person, nor had he received any injection.

Physical examination. He was a frail jaundiced man. His liver was palpable, 5 cms. below the costal margin and was tender, firm and regular. The gall-bladder was not palpable. Results of special investigations were as follows: Plain X-ray of the gall-bladder area was normal; Wasserman test, negative; Casoni test, negative; serum bilirubin, 24 units; cephalin flocculation, negative; prothrombin index, 78 per cent.; alkaline phosphatase, 45 units; blood urea, 53 mg. per cent.; bile salts and urobilin present to excess in urine. Liver biopsy report was "biliary obstruction with early biliary cirrhosis."

After forty-eight hours' intravenous therapy, the patient was considered fit for operation.

Operation for drainage, 19th Jan., 1953. Through a subcostal incision, the liver was found to be enlarged and cirrhotic, neither the gall-bladder nor the common bile duct was distended. An elongated tumour 1 cm. long was palpable in the porta hepatis. There were no obvious metastases. The common bile duct was opened and a sound passed upwards beyond the tumour and easily into the left hepatic duct. However, it could not be manipulated into the right hepatic duct. When it was withdrawn a large quantity of "white bile" was released. A soft rubber catheter was then passed upwards past the tumour and sutured in position. A larger drain tube was placed in Morison's pouch and the abdomen closed.

Post-operative period. "White bile" changed to normal bile, there was a clinical decrease in the jaundice, gain in weight and well-being, until on 9th Feb. the serum bilirubin was 4 units, the cephalin flocculation was negative. The prothrombin index was 76 per cent. and the alkaline phosphatase, 27 units.

Operation for excision, 9th Feb. Through a thoraco-abdominal incision, the liver was mobilized and rotated upwards into the thorax. The hepatic artery, portal vein and bile ducts were identified and the hepatic ducts mobilised up into the porta hepatis. The supra-duodenal portion of the common bile duct, the gall-bladder and the distal 0.5 centimetre of the right and left hepatic ducts were excised above the level of the tumour. A Roux-en-Y anastomosis was then performed between the jejunum and the open ends of the hepatic ducts. The specimen removed was an adenocarcinoma of the junctional region of the right and left hepatic ducts; it almost completely filled the lumen.

Post-operative period. The patient was very ill on return to the ward and despite resuscitation he remained moribund, passing very little urine. He died three days after the operation.

Post-mortem examination showed an area of infarction of the liver which occupied about one-twelfth of the liver substance. However, the hepatic arteries and portal veins appeared normal. There was some bile stained lymph around the anastomoses but no general peritonitis. The right pleural cavity contained some blood stained fluid but the lung contained air except for an area of the right lower lobe which was collapsed and congested. No metastases were found.

CONCLUSIONS AND SUMMARY

1. An operative technique for the surgical approach to the porta hepatis is described.
2. Two patients are reported in whom excision of carcinomata of the junctional region of the hepatic ducts was performed. One patient, a male aged 35 years, has remained in good health, without jaundice, for a period of eight months. The other, a male aged 74, died from liver failure following infarction four days after excision of the tumour; post-mortem examination revealed complete removal of the tumour and no evidence of secondary deposits.
3. Our experience greatly encourages us to recommend bold removal of these tumours, following a preliminary drainage of the ducts to improve liver function and decrease the size of the liver.

ACKNOWLEDGEMENTS

We would like to thank Dr. W. E. King and Dr. Ian Wood for their assistance in diagnosis and management of these patients. The preparation for operation and resuscitation was supervised by Dr. E. B. Drevermann.

THE DEVELOPMENT OF MALIGNANT MELANOMA IN BOTH RECIPIENT AND DONOR SITES OF AN AUTOGENOUS SKIN GRAFT

By H. A. S. Van Den Brenk

Melbourne

A CASE is here recorded, in which an autogenous skin graft was followed by simultaneous development of malignant melanoma in both the site from which graft was taken, and in the transplanted piece of skin. This must be a rare and perhaps a unique event. A review of the literature on cutaneous melanoma, whilst by no means complete, has failed to show a similar occurrence. The case is reported in detail and some observations are made in reference to the bearing this particular case has on the pathology of malignant melanoma, particularly in reference to tumour genesis.

Case Report

Eighteen months prior to admission to hospital on 10th November, 1952, a male, aged 68 years, developed a paronychia of the right thumb. The nail was removed but poor healing took place. A skin graft was then taken from the volar surface of the right forearm and applied to the unhealed area in the nail bed. Healing however, was still poor and nine months later, the nail bed of thumb and distal phalanx were removed, a skin flap was fashioned and thrown back over dorsum of thumb.

FIG. I. Photograph taken pre-operatively showing pigmented tumour nodules on the forearm and the thumb.

Healing now took place, but patient noted that soon afterwards, two small dark spots appeared in the scar on thumb. Furthermore, at the donor site on forearm, normal healing never occurred but an abnormal wart-like appearance developed and about six months prior to admission to hospital, the area became dark in colour. This area was now excised and good healing occurred.

About three weeks prior to admission, however, the scar of donor site broke down with the development of several dark blebs along length of scar, the distal one of which enlarged rapidly and became mushroom shaped. At the same time the two dark spots on the thumb scar also enlarged and became ulcerated.

The patient could not recall the presence of a mole in or near the donor area on his forearm.

Clinical examination

Volar surface of right forearm. A longitudinal scar was present and situated in its centre, a protruding nubbin of tissue 2.2 x 1.2 x 0.5 cm. in size, with a smooth surface, slightly pedunculated and bluish-black in colour. Distal to this tumour, along the length of scar, three similar, but smaller, raised pigmented nodules were present (Figs. I and II).

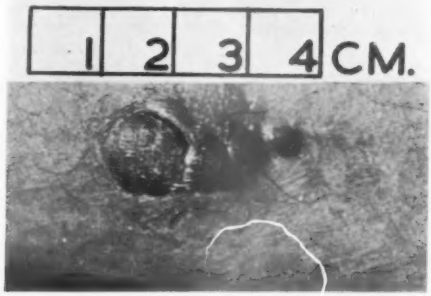

FIG. II. Photograph of tumour on the skin of forearm (donor site). The nodules are situated along the length of a scar.

Right thumb. The distal phalanx was largely missing, and situated on a dorsal scar were two rounded ulcerated areas, bluish-purple in colour, not fixed to the underlying tissues, and measuring 1.2 x 1.0 x cm., and 1.0 x 0.5 cm., in size (Figs. I and III).

Lymph node areas. There was no clinical enlargement of the epitrochlear, axillary or supraclavicular lymph nodes.

Liver. No signs of enlargement.

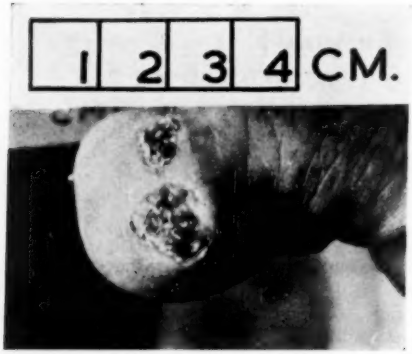

FIG. III. Photograph of the recipient site, showing the growth of tumour nodules along the scar of a previous amputation.

Investigations

X-ray examination of chest. Lung fields clear.

Biopsy. On 13th November a small superficial fragment of tumour on the forearm was removed by means of a diathermy loop.

Pathological report (Dr. J. D. Hicks): "Masses of spindle-shaped cells in strands of fibrous tissue are present. A good deal of brownish pigment is present mainly at the edges. Some of the cell groups are quite irregular, the masses being closely packed. Malignant melanoma."

Treatment

On 26th November, 1952, Mr. A. E. Coates, performed an interscapulo-thoracic amputation. Convalescence was uneventful.

An examination of the operation specimen showed malignant melanoma to be present in both the forearm and the thumb, confirmed microscopically.

There was considerable deep extension of tumour into the forearm, but the axillary nodes examined were not involved in tumour spread.

DISCUSSION

The origin of a malignant growth in a cell population, in the event of an adequate stimulus being applied to competent cells in a suitable environment, has received much attention, owing to its great importance from both a theoretical and practical aspect.

Willis (1948) states: "A skin cancer in its early formative stage arises more by general transformation of pre-existing epidermis than by cellular multiplication and only after the formative field has all suffered neoplastic change does the tumour grow by multiplication. The two processes, neoplastic transformation and proliferation, overlap, the former predominating during the early genesis of the tumour, the latter often being initially negligible, but gradually taking an increasing and finally exclusive part in the growth of the tumour."

This conception of multicentric origin of a tumour in a formative field dates from the observations of John Hunter and is based largely on histological studies, particularly those of Cheatle (1921) and Nicholson (1921) in breast cancer, Dawson (1925) of cutaneous melanoma and the detailed histological sequences observed by Deelman (1923) in skin exposed to carcinogenetic hydrocarbons.

Although the histological evidence is convincing and largely accepted to-day as proof that numerous cells participate simultaneously or within a comparatively short space of time in malignant transformation, there are still observers who favour a unicentric hypothesis. Thus Ewing (1940) states: "These instances of lateral extension of tumour processes, if they eventually stand the test of criticism, are rare and it should be emphasized that the great majority of tumour cells are isolated in origin and throughout their history."

Furthermore, despite Cheatle's (1921) classical studies of the sections of whole breasts and his demonstration of multifocal change, it is nevertheless a common clinical observation that there is rarely more than a single primary malignancy present in a given organ. Thus, whilst actinic cancers of the skin are sometimes multiple, the vast majority of patients present with a single tumour in a field which has been subjected very uniformly to the carcinogenic agent, namely, ultraviolet light. Furthermore, the recent studies by Foulds (1951) of the life history of artifically induced tumours, demonstrates that "progression" usually takes place in a circumscribed area, with the development of a single malignant tumour in a prepared field. Mottram (1935) studied the problem by quantitative estimations of tumour growth induced in mouse skin by 1:2:5:6 dibenzanthracine. He extrapolated the log of the area curve graph against time, back to the time of first application of the carcinogen, and found that the tumour must have begun within a day or two of the first application and from an area about the size of a single cell. However, this hypothesis is open to the

obvious criticism, that the rate of growth of a tumour would of necessity be proportional to both latent period and the potency of the carcinogen, a pre-requisite not substantiated experimentally.

The more recent experimental work of Berenblum (1941) and Mottram (1944) on the part played by specific "initiation" and non-specific "promotion" in the genesis of malignancy in a cell population, seems to be of great significance in this regard. In the particular case reported here, artificial autogenous transplantation of a piece of skin has been followed by malignant progression in both donor and recipient sites. The assertion of both patient and surgeon that no pre-existing lesion was present at the time of skin grafting cannot be ignored. The development of malignancy in both donor and recipient sites certainly suggests that numerous cells spread over a wide area must have already undergone a specific "initiation" at the time of grafting. However, malignant progression did not occur at both sites till a further period of approximately nine months.

It is therefore suggested that the trauma of transplantation in itself was not an adequate "promotor," but possibly nutritional changes, resulting from scarring at both sites, may have provided the necessary stimulus. Such a hypothesis recalls the observations of Orr (1938), who drew attention to the importance of stroma and tumour bed in the development of epithelial tumours.

This worker, in a histological study of invasive carcinoma, drew attention to the close relationship of developing carcinoma and dermal scars and damaged elastic tissue.

Whether or not the cells of outlying competent tissues which have been subjected to the same adequate specific "initiating" stimulus (for example in actinic cancer) as the area developing progressive malignancy, that is, the active neoplasm, lack the non-specific "promoting" stimulus, it is difficult to answer. An alternative explanation, suggested by the work of Foulds (1951), draws attention to the possible inhibitory influence a growing tumour may have on both the rest of the prepared field and also any metastatic deposits. Such an hypothesis is certainly enhanced by both the oft seen recurrences in a formative field after successful treatment, for example, recurrences of buccal cancer after irradiation (Wood and Boag, 1950), and also in the rapid clinical progression of secondary deposits often noted following surgical ablation of a primary growth. However the experimental demonstration of the existence of inhibitory trephones secreted by tumour cells awaits confirmation. The rate of progression of the dual malignant melanomata in the case reported is inconclusive in this regard, although the lesion on forearm was growing much more rapidly than that on the thumb.

A further aspect of this case, which is cogent to the question of development of malignant melanoma, pertains to the incidence of a pre-existing mole in malignant melanoma. A recent review by Hall *et alii* (1952) of the larger series of these tumours shows that estimations of such incidence vary greatly (see Table 1—values of from 18 per cent. to 83.5 per cent. are recorded).

TABLE 1

Showing the Incidence of Recorded Pre-existing Mole in Patients Developing Malignant Melanoma

Author		Number of Cases Reviewed	Percentage of Patients with Pre-existing Mole
Affleck	(1936)	317	83.5 per cent.
Daland and Holmes	(1939)	174	18 per cent.
Webster *et alii*	(1944)	104	65.4 per cent.
Ackerman	(1948)	75	61. per cent.
Hall *et alii*	(1952)	159	70.4 per cent.

Whereas Daland and Holmes (1939) found an incidence of only 18 per cent. in 174 cases examined, and consider that many melanomata are malignant from the commencement, Pack (cited by Hall *et alii*, 1952) goes to the other extreme and points out that the average individual has twenty visible pigmented moles but, on questioning, will deny the presence of a single mole on his person; he goes so far as to suggest that every melanoma originates in a quiescent pigmented lesion of the junctional naevus type.

In this particular case it is almost certain that there was no visible pigmented lesion present; both from the assertions of patient and surgeon and the unlikelihood that the surgeon would have selected such a lesion as the donor tissue for a limited skin graft, with choice of the whole arm for material.

SUMMARY

1. A case of malignant melanoma developing in both donor and recipient sites of an autogenous skin graft is reported.

2. Some aspects of this case are discussed, in reference to possible bearing on tumour genesis.

ACKNOWLEDGEMENTS

My thanks are due to the Cancer Institute Board, Melbourne, and the Honorary Staff of the Royal Melbourne Hospital for permission to make this report and to Dr. G. R. Kurrle for first drawing my attention to this case.

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Books Reviewed.

MIDDLE EAST AND FAR EAST.

By ALAN S. WALKER, M.D., Ch.M., F.R.A.C.P. Canberra: Australian War Memorial, 1953. 9¼" x 6", xvi plus 702 pp., 110 illustrations. Price: 35s.

This volume is the second of the Medical Contributions (Series five) in the group of Official War Histories dealing with various aspects of the Army, Navy and Air Force during the 1939-1945 War.

Like the preceding volume, it covers a very large field geographically and deals with the period of the war up to 1942.

The management of such a wealth of what is, in many cases, only slightly related material and its integration into an ordered narrative is again a matter for congratulation of the writer. In many ways the touch here is surer and the matters are dealt with with obvious knowledge and understanding of the conditions, so that this volume is even an improvement on the previous one.

It is divided into two parts: the first discusses the formation of the 6th, 7th, 8th and 9th Divisions of the A.I.F. with their general training and organization in Australia and overseas and with the campaigns in the Middle East.

Part two deals with the return of the 6th and 7th Divisions to Australia and with the fate of the defence forces occupying the islands at the north of Australia, and of the 8th Division in Malaya. The two parts of the book are necessarily different and distinct and, indeed, they would be expected by participants in the events to be as different as the desert is from the jungle.

These constitute, therefore, two stories and these are very well told. They will bring back memories to many of those who were present and they will recognize the authentic touch. To all who are interested, they constitute a mine of valuable information dealing with all aspects of the medical services in these two areas.

The volume is bound and printed in the same manner as the previous one, and the material is very well presented. As in the previous volume the illustrations and diagrams are not numbered nor are they adequately referred to in the text. The index here is more satisfactory than in the first volume. In general, this volume is rather better and more coherently presented than the first volume (doubtless because the range of subject permits this) and it is a book which must be read and consulted by all those interested in the medical services during the last war.

THE MANAGEMENT OF ABDOMINAL OPERATIONS.

By RODNEY MAINGOT, F.R.C.S. London: H. K. Lewis and Co. Ltd., 1953. 10" x 6½", xiii plus 1253, 328 illustrations. Price: 120s.

"The Management of Abdominal Operations" is the title of a twelve-hundred page surgical textbook. It comprises 47 monographs, each of which deals with an important phase of the management of abdominal operations, and each of which is written by a specialist distinguished in his subject. It is nice to see that the book is dedicated to Lord Webb-Johnson who, in so many ways, has done so much for British surgery. The work is edited by Rodney Maingot who is also responsible for some of its ablest articles, and is divided into three parts.

In general, its character is in keeping with the present surgical era in that there is a medico-biochemical side to this practical surgical book. This is seen in the fact that the first four hundred pages are devoted to the medical aspects of surgery; to those epoch-making advances in medicine of recent years which, when applied to the practice of surgery, have so greatly increased its efficacy. Obviously the spirit underlying this section is to legislate for team-work in surgical practice.

In Part II the approach is from the operation side. And in Part III, a very short section, it is along the lines of modern aseptic surgical technique, of advanced hospital procedure and of new standards in pathological values in health and disease.

Part I is perhaps the highlight of the book because it not only breaks much new ground in its exposition of the scientific principles involved in the non-operative management of abdominal operations, but also because it integrates the many aspects of this management into systematized methods based on medical and biochemical findings, and because it describes not only practical but also adequate details for the precise application of these methods

In this part there are eighteen monographs covering the pre- and post-operative management of abdominal cases, each of which is authoritative, comprehensive, ably written and the last word on the subject.

The subjects of the monographs are as follows: Anaesthesia, Water balance, Nutrition in surgical patients, Shock, Blood transfusion, Venous thrombosis, Pulmonary complications, The use of chemotherapeutic and antibiotic agents, The role of vitamins, The conditions affecting operative risks, The non-operative management of the acute abdomen, and The methods employed in preventing or combating troublesome or lethal post-operative complications.

The surgeon who studies these monographs will come away with (a) some of England's best scientific medico-surgical thought; (b) with knowledge which will enable him to resolve into components the critical pre- and post-operative problems; and (c) with the mental equipment capable of organizing and leading a team which will practically adapt this therapy to the particular rehabilitation or resuscitation problem.

The feeling running through these monographs is that seriously debilitated patients still die unnecessarily—(a) because the great potentiality of this present-day therapy is not fully recognized; or (b) because, if it is recognized, it is empirically administered; there is inadequate investigational data on which to base and, therefore, specifically to apply the therapy. A case in point is the empirical

administration of whole blood instead of "packed" red corpuscles in an acute emergency in which anaemia is the obvious feature, but in which there is also a cardiac but undetected factor which becomes the cause of death.

In Part II the approach to the subject of the book is from that of the fruits of a wide knowledge, in terms of judgment, of the master surgeons of England who write the monographs in this section. These monographs cover nearly every abdominal operation problem which has, in recent years, come under the limelight of criticism or the test of experience. Thus, the reader sees the management of abdominal operations from an entirely different angle: from that of the operation in actual practice by the finished surgeon.

The book is well illustrated both from the operation and the investigational (X-ray) point of view.

This work could well be open to some criticism in that there is a certain want of uniformity and a certain degree of repetition. But this is inseparable from a book such as this. Indeed it is more than counterbalanced by the value of the single-minded, gently pruned approach to the various subjects, with the author at home and more explicit in his own particular style.

To the surgeon at the summit of his career, this book will group his knowledge in the medico-surgical advances of recent years. To the surgeon who is ascending in the profession, it has a particular value. To the senior resident medical and surgical officers and the Fellowship candidate, it is an essential. And to the ambitious student, it could well be a background to his standard educational efforts.

The book, published by H. K. Lewis and Company, more than maintains the high standard of the English medical publisher.

PATHOLOGY OF TUMOURS.

By R. A. WILLIS, D.Sc., M.D., F.R.C.P. Second Edition. London: Butterworth and Co. Ltd., 1953. 9¾" x 6¼", xiv plus 1051 pp., 500 illustrations. Price: 114s.

That there should have been two reprints and a second edition of this book in the five years since the first edition appeared is clear indication of the general appreciation of its value.

There have been relatively few changes in this edition. Some of the subjects such as the experimental production of tumours and sections on certain special tumours have been changed or rewritten. There have been a few alterations to the illustrations and about 400 references have been added to the bibliography.

There is little to be said beyond what was stated originally regarding the first edition. To those who are not well acquainted with this edition, this book is strongly recommended as an excellent contribution to our knowledge of the subject of tumours, tendered from the point of view of an investigator who has made a life-long study of the diseases.

The material is very well presented and the various points of view of the writer are put forward in his inimitable fashion. Even where one does not always agree with the view point, there is no doubt about the opinion of the author; it is so clearly stated that it is easy to accept or reject according to one's own point of view or information.

The high standard of presentation of text, illustrations and material generally are a credit both to the author and the publishers. This book is recommended to all those who are interested in the subject of tumours.

BRITISH SURGICAL PRACTICE: Surgical Practice for 1952.

By Sir ERNEST ROCK CARLING, F.R.C.S., F.R.C.P., and Sir JAMES PATERSON ROSS, K.C.V.O., M.S., F.R.C.S. London: Butterworth and Co. Ltd., 1952. 10" x 6¾", vii plus 340 pp., 81 illustrations. Price: 58s. 6d.

Surgical Progress for 1952 is the second of an annual series of supplementary volumes to *British Surgical Practice* and this volume is of the same high standard as the eight main volumes in appearance, presentation and material. The ever increasing field of surgical knowledge is brought up to date in three ways—by original articles, critical surveys and abstracts of current literature.

In the six original articles, the treatment of chronic arthritis, burns, malignant exophthalmos, heart surgery, restorative resection of the rectum and the vascular supply of the stomach are discussed. These chapters are extremely well written, particularly that on burns in which the exposure method of treatment receives due recognition. Heart surgery is described in a general way, but in a volume such as this its value is doubtful since the thoracic surgeon will find little of interest to him. The vascular supply of the stomach in relation to gastric ulcer is a fine example of original investigation.

In the critical surveys, modern anaesthesia, hypertension, pre-frontal leucotomy, the surgery of the intestines and chronic oedema of the leg are discussed. In each of these chapters the present position of surgical knowledge is set forth admirably.

The last portion of the book contains abstracts of a wide range of current surgical literature. The "Noter-Up" section which follows enables subscribers to the main work to find all the recent relevant information on any subject.

It should be realized that this book can be used either independently or as a supplement to the main work and the general surgeon will find in it a great deal of new information. There is no doubt that this book will have a wide circulation both to subscribers and non-subscribers of *British Surgical Practice* as it represents all that is best in British Surgery to-day.

MODERN TRENDS IN DIAGNOSTIC RADIOLOGY (2nd Series).

By J. W. McLAREN. London: Butterworth and Co. Ltd., 1953. 9¾" x 6½", xi plus 413 pp., 35[illegible] illustrations.

The bloom and freshness of a good first text book are like the view of a familiar and attractive landscape from a new aspect. After Dr. McLaren produced his "Modern Trends in Diagnostic Radiology" in 1948, it rapidly became a popular

resort for radiologists studying the by-paths of their special territories. In this, his second series, he has not redecorated the old scenes, but has furnished us with guides to other avenues. The freshness has been sustained.

The chapter on "Volume Dosage in Diagnostic Radiology" is of particular interest because it warns of the dangers of exposure to X-rays. When so many medical practitioners other than radiologists have their own equipment, a large number of patients have duplicated X-ray examinations. An appreciation of the danger of over-dosage cannot be impressed too strongly on all who examine patients with X-rays, particularly when so many who use this insidiously destructive medium have no clear idea of dosage limits. Reasonably accurate data of doses of X-rays given to patients should be kept by all users of X-rays and made available to those who may subsequently X-ray these same patients.

Specialist surgeons and physicians now have become so familiar with the intimate details and nuances of radiology in their specialties that those who have a particular interest in diseases of the chest, neurology, urology, and orthopaedics and other branches of medicine and surgery will find much to interest them in this volume.

The investigation of the dynamics of the heart by synchronised serial angiocardiography (10 pictures per second) and a standard lead for electrocardiography, opens up a bright prospect for the determination of borderlines between the normal and the pathological. In the chapter, too, on "Selective Angiocardiography and Thoracic Aortography," the subjects are very well presented both as to letterpress and reproductions. Stress is laid on the fact that in adults the permissible quantity of opaque medium must be concentrated where the problem is to be solved, because it is difficult to obtain satisfactory density of medium in the entire intrathoracic circulation. Concurrent electrocardiograms should be taken.

An exhaustive study of methods of examination of the colon emphasizes the difficulties and fallibility of a radiological examination which produces many false conclusions of both a negative and a positive kind. Two dicta may be quoted as the alpha and omega of the examination of the large intestine. "It is of prime importance that the caecum be positively identified in every case" . . . and "We (radiologists) have never accepted responsibility for diagnosis of lesions in the rectum."

Air studies of the skull and cerebral angiography are spaciously treated with technique and anatomy receiving most consideration. The names of E. G. Robertson and J. B. Curtis have their due recognition in these fields.

One reads with great interest that myelography has increased sevenfold at the Manchester Royal Infirmary in the past four years. The reviewer's observations lead him to believe there has been a marked local decrease in myelography in the past few years. An examination such as myelography reaches its zenith of usefulness when clinicians can more and more frequently make accurate diagnosis from the clinical signs and symptoms only. Extensive studies of these, correlated with pathological specimens and X-ray examinations lead to a gradual decline in the necessity for the X-ray examinations.

Contradictory statements are made concerning myelography. Reasons given for the increase in Manchester include, "the realization that myelography is safe, (&) does not usually upset the patient . . ." On the next page we find, "Meningism and slight fever is (sic) not uncommon after myelography," and "adhesive arachnoiditis may well be commoner than has been supposed." Enthusiasm and efficiency may make myelography more popular, but this examination should not be undertaken lightly. Those who nurse patients after myelography know best how much or how little it upsets patients.

A sketchy review such as this cannot adequately emphasize the usefulness of the book for reference. Its chapter headings should be delved into and applicable ones noted by the individual connoisseurs. It is the radiologist's vade-mecum and its contents are a common talking ground for him and his specialist confrères.

DISEASES OF THE NOSE, THROAT AND EAR.

By F. W. WATKYN-THOMAS. London: H. K. Lewis and Co. Ltd., 1953. 9¾" x 6½", xvi plus 880 pp., 367 illustrations, 22 in colour. Price: £5 10s. net.

This book of 880 pages with 367 illustrations, including 22 coloured plates, was apparently primarily conceived in order to bring up to date the last edition of Herbert Tilley's handbook on diseases of the nose and throat. There are eleven contributors to the work edited by Watkyn-Thomas, nearly all having some connection with University College Hospital, London. Part I deals with special methods in the nose, throat and ear; Part II with the larynx, hypopharynx, trachea and oesophagus including endoscopy; Part III with the oropharynx and nasopharynx; Part IV with the diseases of the nose and accessory nasal sinuses, and Part V with the ear. If one can criticize in a friendly fashion one's old teacher and master, I would say that it is a pity he did not write a textbook on diseases of the ear alone, as he did in the 1920's. The parts he has written are well nigh perfect as our knowledge stands to-day and they are so beautifully balanced and so clearly written that they could only have been written by an observant scholar of long and rich experience. In the remainder, many of the sections are sketchy and the post-graduate student would have to look elsewhere for a sound knowledge. There are some typographical errors, but these are below the normal expectation. In the section on physiotherapy one is pleased to see a warning against the use of short-wave diathermy in an acutely infected antrum or accessory nasal sinus with a blocked ostium; also the reference to the fact that little carefully controlled work has been recorded in the literature of recent years and therefore much of the treatment advocated in this field is based on clinical impression rather than on scientific fact or statistical results. In corrosive injuries to the oesophagus, neither of the American methods are described, e.g., Tucker's bougies, or Jackson's dilation by bougienage. In Part III, retropharyngeal abscess, and especially lateral pharyngeal abscess and Ludwig's angina are done well. The

section dealing with indications for tonsillectomy is in general well covered, but some of the points are arguable. Removal of tonsillar tissue by diathermy is rightly frowned upon because infected crypts are enclosed and their drainage lost and risk of toxic products being absorbed into the bloodstream is increased. The hypothesis that the tonsils act as filters for organisms passing through the fauces is surely a relic of the past. The discussion on tuberculosis of the pharynx and fauces is good and informative. Treatment of bleeding from the adenoids (really what is meant is bleeding after the removal of adenoids) is well covered. It is pleasing to see a statement that secondary haemorrhage after removal of tonsils occurs as the result of infection of the tonsillar fossa. The discussion on the juvenile fibro-angioma of the nasopharynx is good. In the chapter on allergy in the ear, nose and throat, the principles rather than any details are foremost. The reviewer agrees that the basic condition in nasal polypi is a non-suppurative chronic ethmoid sinusitis but finds it hard to agree that "the individual polypi are yellowish white, semi translucent mucosal cysts containing oedema fluid." There may be fluid spaces or even small cysts but by and large nasal polypi are not cysts as such. Chapter 54 on the treatment of nasal sinusitis and its complications is really practical and useful. In discussing the Caldwell-Luc operation, mention is made of the fact that any mucosa that seems to have a reasonable chance of returning to normal is left intact. Ruthless stripping is avoided. This advice may be misunderstood and misapplied by the inexperienced. The discussion on the relative merits of the Jansen-Horgan operation, the Ferris-Smith operation and the Norman-Patterson operation and the details of these operations is particularly clear and useful to the younger members of the specialty. Without entering into a long discussion on the relative merits of the different procedures for surgical drainage of the frontal sinus, I would say that in my experience obliteration of the frontal sinus was a more successful procedure than Suggitt indicates, even making allowance for the fact that it is a difficult thing to achieve in the very large well-pneumatised frontal sinuses. With regard to osteomyelitis of the skull, larger doses of penicillin than mentioned continued for a longer period of say five to eight weeks have been found necessary in my experience.

In the chapter on cysts and tumours of the upper jaw and nasal sinuses cysts of dental origin are given very little space which seems a pity, classification of these tumours is usually hazy in text books, and confuses the student, both undergraduate and graduate. In treatment of malignant tumours of the upper jaw and antro-ethmoid areas I agree with the statement that combined surgery with diathermy and irradiation gives better results than either surgery or irradiation alone. Irradiation is given before and, if necessary, after surgery.

Part V deals with the ear, and is a first-class account of the subject in all its aspects. In chronic suppurative otitis media the author states that the "migration" hypothesis for cholestestoma is untenable nowadays and describes a number of other hypotheses but does not make it quite clear what he thinks the migration of squamous epithelium through a perforation replacing less differentiated cubical or even less differentiated squamous epithelium cannot occur. Nevertheless the whole question is discussed fully and well. Mastoid operations are very well described and only minor points could be argued, for example, in the radical, nowadays, with the use of magnifying operating spectacles, and the crook ended dental scaler, in most cases one can safely lift up and strip the mucosa in a sheet from the wall of the tympanum. It is agreed that one never curettes the inner wall. It is agreed that the area of the oval window with the stapes in situ should be very cautiously treated and in fact, largely left alone, but in my experience the mucosa of the inner wall if it is lifted up by the method mentioned and grasped by antral polyp forceps often strips over the stapes without damage to this area. It is depressing to hear that such an experienced aural surgeon as Mr. Watkyn-Thomas regards the Eustachian tube as impossible of closure. In probably what is one of the best chapters on the description of mastoid operations extant, it is a pity that mention was not made of the extended Schwartze type of operation which has recently been given fresh publicity by Daggett. In the appropriate case the reviewer feels that this is an operation which is excellent in its results and has a permanent place in mastoid surgery. This book is worth a place on any library shelf for the aural section alone.

Books Received.

SURGERY OF THE BILIARY TRACT, PANCREAS AND SPLEEN.

By CHARLES B. PUESTOW. Chicago, U.S.A.: Year Book Publishers Inc., 1953. 8¼" x 5¼", 370 pp., 72 illustrations. Price: $9.00.

REVIEW OF PHYSIOLOGICAL CHEMISTRY.

By HAROLD A. HARPER. Fourth Edition. California, U.S.A.: Lange Medical Publications, 1953. 10" x 6¼", 328 pp., 27 tables. Price: $4.00.

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